AUGUST, 1951

The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

Acute Cholecystitis and Biliary Tract Disease

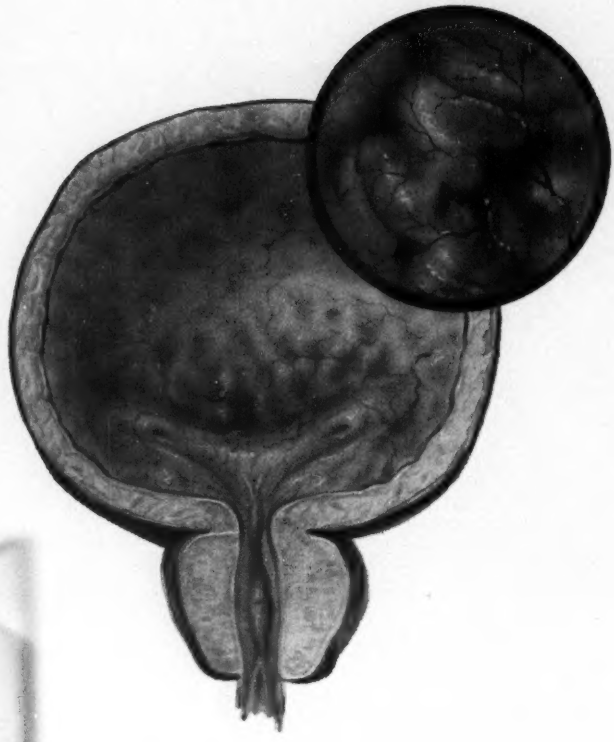
Surgical Therapy for Gastrointestinal Hemorrhage in Portal Hypertension

Nonspecific Regional Jejunitis

●

Sixteenth Annual Convention
Chicago, Ill., 17, 18, 19 September 1951

VOLUME 18 NUMBER 8



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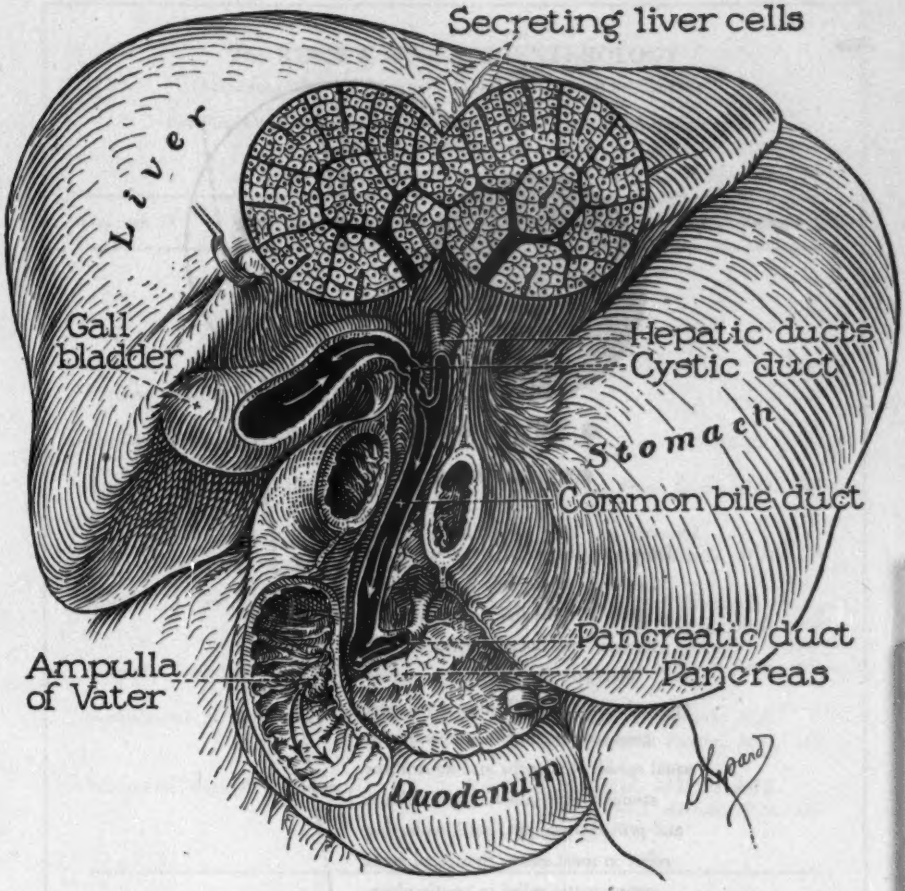

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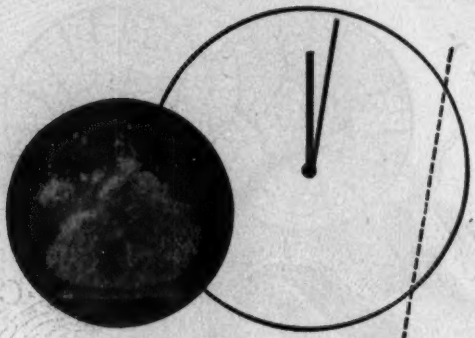

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The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

VOLUME 18 AUGUST, 1951 NUMBER 8

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of the

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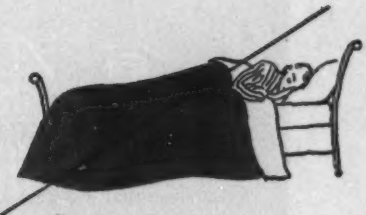

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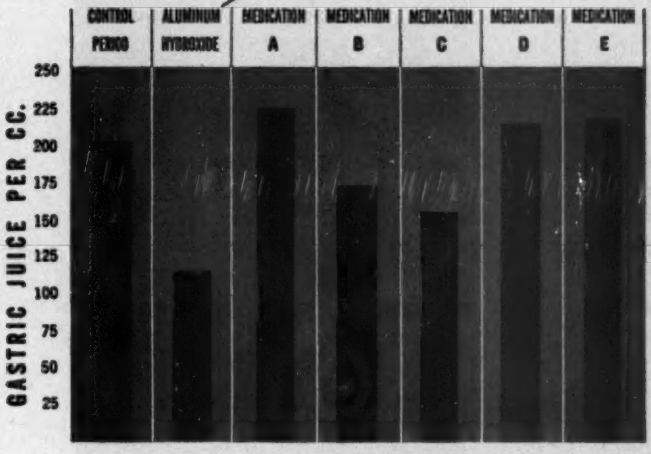

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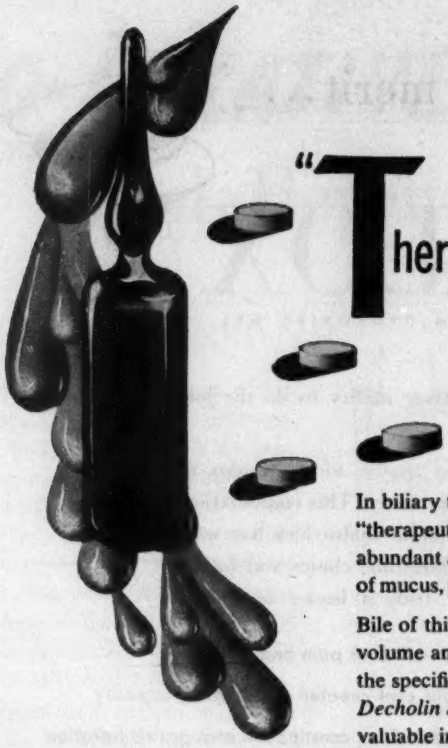

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ACUTE CHOLECYSTITIS AND BILIARY TRACT DISEASE*†

FRANK GLENN, M.D.

New York, N. Y.

H. E. Robertson[1,2] has estimated that 40 per cent of the female population of the United States who are over fifty years of age have gallstones. It is generally agreed that the presence of gallstones indicates disease of the biliary tract. At The New York Hospital—Cornell Medical Center, almost 3,500 patients with cholelithiasis have been treated surgically over the past 18 years. Eighty per cent of these patients have been women, and three out of every four female patients had been pregnant at least once. Many of these patients gave a history of recurrent attacks of acute cholecystitis. Biliary tract disease is a common entity in our population, and until we know how to prevent its development it is necessary that we make every attempt to interrupt its progress as early as possible as well as relieve the symptoms associated with it. Early surgical treatment of this condition has many advantages over the conservative medical management that was so commonly advocated a quarter of a century ago and still is followed by some. It is these advantages that are to be presented here for your consideration. Their achievement marks the evolution of the modern concept of treating biliary tract disease by surgery.

Those who first advocated the early surgical treatment of acute cholecystitis did so in an attempt to avoid the immediate complications of perforation, namely, local or generalized peritonitis. Relief of symptoms and prevention of later attacks was scarcely mentioned, but follow-up studies on patients treated by cholecystectomy for acute cholecystitis in early life show that these factors are of clinical significance. Relief of symptoms and prevention of future attacks are commendable accomplishments, but of equal or even greater importance is interruption of the biliary tract disease itself. It is the sequelae to biliary tract disease and its complications that account for its morbidity and toll in mortality. Such complications and sequelae include common duct stone, liver damage, carcinoma of the biliary tract, and changes associated with the cardiovascular system.

Acute cholecystitis, or acute inflammation of the gallbladder, is often superimposed upon a chronic cholecystitis that is associated with cholelithiasis. How-

*Presented before the Course in Postgraduate Gastroenterology of the National Gastroenterological Association, New York, N. Y., 12, 13, 14 October 1950.

†From the Department of Surgery of The New York Hospital—Cornell Medical Center.

ever, the acute phase of the disease may also appear as the primary infection of the biliary tract and it may develop in the absence of stones. In contrast to chronic cholecystitis, the acute type presents the clinical manifestations of an acute inflammatory or obstructive process. Though the acute attack usually subsides, it can progress, and if it does, may result in perforation, abscess formation, or peritonitis, local or generalized. In addition to involvement of the gallbladder, there is almost always extension of the infection to the biliary ductal system, namely, a cholangitis of varying degree. Each episode of acute cholecystitis results in some injury to the liver. We believe that the surgical interruption of such attacks is justifiable, and, following this policy, 729 patients with acute cholecystitis have been treated at The New York Hospital—Cornell Medical Center by early operation during the last 18 years (September 1, 1932 to September 1, 1950). Surgery is embarked upon as soon as the patient is adequately prepared, unless there is some condition present that is not immediately reparable and which contraindicates operation.

Since a large proportion of the patients with biliary tract disease are women who have had one child or more, it is common to obtain a history of symptoms

TABLE I

THE SURGICAL TREATMENT OF 729 PATIENTS WITH ACUTE CHOLECYSTITIS

The New York Hospital
September 1, 1932 to September 1, 1950
(18 years)

Cholecystectomy	640
Cholecystostomy	89
Choledochotomy	62
Deaths	20
Mortality rate	2.7%

dating from the early twenties. Since these symptoms so often include acute attacks, the advantage of early operation is apparent, not only for the acute stage of cholecystitis but for the chronic phase of the disease as well. The fact that we have not had one death from acute cholecystitis in over 18 years in our group of patients under 40 years of age, save for a child who had acute typhoid cholecystitis, is quite significant. It lends support to our contention that biliary tract disease can best be interrupted by surgery soon after its onset.

In our series of 729 patients (Table I), 439 were under 50 and 290 were over 50 years of age. Total deaths for the group were 20, a mortality rate of 2.74 per cent, but the difference in the rate for each group is more significant. In the older group of 290 patients there were 14 deaths, or 4.8 per cent, whereas in the younger group there were only 6 deaths among the 439 patients, a mortality rate of 1.37 per cent. These figures indicate the desirability of reducing the necessity for surgery in the older group. The older patients have a higher incidence of complications that can lead to death from acute cholecystitis if they are not operated upon. The difference between a mortality rate of 4.8 per cent and 1.37 clearly indicates the fact that to operate before the patient reaches the age of 50 will do much to reduce the overall mortality from acute cholecystitis. We do not mean to say that acute cholecystitis

can be prevented after 50, but we do believe that it can be materially reduced if those with acute attacks of cholecystitis undergo operation when they first begin to have them, and if those with chronic cholecystitis and cholelithiasis are treated by surgery early in the course of their disease, preferably before the age of 40. If cholecystectomy can be performed for chronic cholecystitis and cholelithiasis with an operative risk of less than one-half of one per cent fatality, then there can be little justification for medical or nonsurgical management of the disease. Conservative measures only render the disease more tolerable to the patient and permit continuation of its deleterious effects. There is a great need for long term studies to throw light on the etiology and pathogenesis of biliary tract disease and its relation to other systemic changes.

Our 729 patients were treated by cholecystectomy or cholecystostomy, with choledochotomy added in 62 instances. Six hundred forty patients, 87.8 per cent, were treated by cholecystectomy, the procedure of choice. However, this procedure was deemed inadvisable for the remaining 89, 12.2 per cent, and cholecystostomy was employed instead. Cholecystostomy is a compromise procedure, but there are

TABLE II

THE SURGICAL TREATMENT OF 439 PATIENTS UNDER 50 YEARS OF AGE

The New York Hospital
September 1, 1932 to September 1, 1950
(18 years)

Cholecystectomy	400
Cholecystostomy	39
Choledochotomy	31
Deaths	6
Mortality rate	1.37%

times when it should be resorted to without hesitation. When indicated, it may save a life by averting immediate disaster and tiding the patient over for definitive treatment later, when cholecystectomy can be accomplished with much less risk. We reserve choledochotomy for patients with definite evidence of common duct obstruction. Only 62, or 8.5 per cent of the group had this procedure added to cholecystectomy or cholecystostomy. There were 20 deaths in the entire group of 729 patients, an overall mortality rate of 2.74 per cent.

In a carefully studied group of 100 patients with acute cholecystitis that were treated by cholecystectomy and followed for 10 years or more, we found that 88 per cent have remained symptom-free since operation, as far as the biliary tract is concerned. Two patients were found to have common duct stones, which either developed after their cholecystectomy or were overlooked at that time. One patient developed stenosis of the common duct, probably as the result of injury at the time of the cholecystectomy. One patient had attacks of pain later, for which she was explored. A remnant of a cystic duct containing small stones was found and removed, with relief of symptoms. One patient has had recurrent attacks of what is believed to be acute pancreatitis. Two patients have had duodenal ulcers demonstrated by x-ray, but they have been fairly well controlled on a medical regime. One

patient has undergone operation successfully for recurrent bleeding from a duodenal ulcer. We feel that these follow-up results are significant, as they demonstrate for this small series at least only two instances of common duct stone, no case of progressive or extensive liver damage, and no recognized biliary tract malignancy.

Common Duct Stones

It is rare to find stones in the common duct and none in the gallbladder. Generally speaking, common duct stones are an indication of long present biliary tract disease, and, more specifically, stones in the gallbladder. Over a period of 18 years we explored the common duct in 380 patients and removed stones in 56 per cent. We found, as have others, that the incidence of stones in the common duct increases materially with each decade after forty. In our series of 729 patients we found that the incidence of common duct stone was 4.3 per cent for patients under 50 and 7.2 per cent when over that age.

We explore the common duct only on specific indication. By this we mean a history of repeated attacks of jaundice, or progressive jaundice, dilatation of the common duct, stones palpable within the duct, or the presence of pancreatitis. Adhering to these indications, we have found from our ten-year follow-ups that we have overlooked stones needing removal later in approximately 2 per cent of the cases.

Choledocholithiasis is a more serious condition than stones in the gallbladder. The morbidity and mortality associated with choledocholithotomy is higher than for cholecystectomy for chronic cholecystitis and cholelithiasis for several reasons. First, the patient with choledocholithiasis is generally older. Second, as McCallum[3] pointed out a number of years ago, these patients have a greater incidence of other associated systemic changes, such as cardiovascular disease and liver impairment. Third, choledocholithotomy is a more formidable operation than simple cholecystectomy. Finally, the bleeding tendency associated with liver damage is more pronounced. Because of these conditions commonly associated with choledocholithiasis, choledocholithotomy, though an operation of greater magnitude, is done for a greater proportion of "poor risk" patients than is cholecystectomy. Therefore its higher morbidity and mortality rate.

The fact that stones in the common duct are of greater concern than stones in the gallbladder is best proved by a comparison of the mortality figures. As given above, the mortality rate for our 729 patients treated by surgery for acute cholecystitis was 2.74 per cent. For the 290 patients in this group over 50, however, the mortality rate was 4.8 per cent, whereas for the younger group of 439 under 50 it was only 1.37 per cent. The mortality for a series of almost 3,500 patients operated on for nonmalignant chronic biliary tract disease was 1.8 per cent. In our group of 380 patients subjected to exploration of the common duct, however, there were 26 deaths, a mortality rate of 7 per cent. The period of disability experienced by this group is also significant. These patients with common duct obstruction and considerable liver damage are an unhappy group and are likely to be subjected to long periods of disability. Therefore, avoidance of liver damage

and its associated conditions is highly desirable. Since we are not always able to remove the common duct stones at the primary operation, nor can we always do an adequate repair on the duct with a stricture in spite of all modern facilities available today, every attempt should be made to prevent the development of these complications of biliary tract disease.

Liver Damage

Careful studies of postmortem material have demonstrated that changes in the liver and bile ducts of patients that are known to have a long history of symptoms referable to the biliary tract are often proportional to the duration of the disease. The older the patient and the longer the history of biliary tract disease, the more pronounced these symptoms are apt to be. Similar gross and microscopic findings are seen at autopsy in patients who are found to have had "silent stones" and yet had no recorded clinical history suggesting them. Cholangitis is the basis of these changes. This inflammatory processs takes place within and about the walls of the bile ducts, both intra- and extrahepatic. It may

TABLE III

The Surgical Treatment of 290 Patients 50 Years of Age and Over

The New York Hospital
September 1, 1932 to September 1, 1950
(18 years)

Cholecystectomy	240
Cholecystostomy	50
Choledochotomy	31
Deaths	14
Mortality rate	4.8%

vary from a simple acute reaction with slight lymphocytic and polymorphonuclear leucocytic invasion of the cells of the bile ducts, the liver parenchyma, and the reticulo-endothelial cells, to an extensive scarring of a biliary cirrhosis. Within this range, a suppurative cholangitis may develop and death result. On the other hand, the liver does withstand repeated injury well, and regeneration may take place to a remarkable degree. Numerous factors are involved in the course of this process. As Ravdin[4] has so ably pointed out, the incidence of disabling fibrosis of the liver associated with infection and obstruction is furthered in the presence of certain dietetic deficiencies that sometimes result from dietary restrictions.

In the ordinary course of events, there are repeated episodes of inflammation with or without obstruction in the gallbladder or common duct following the formation of gallstones. With these episodes there is an extension of the process involving the walls of the bile ducts and the portal spaces of the biliary system. The greatest degree of involvement is seen in the patient with common duct obstruction due to stones and a suppurative cholangitis. A patient subjected to repeated acute attacks of cholecystitis readily demonstrates the process that goes on. Following such an attack, reparative processes may correct the injury that has taken place. In contrast is the patient with only mild symptoms but which are

persistent and accompanied by a continuing process of liver damage. This mild but chronic condition may produce a greater degree of liver impairment than do the acute attacks over an equal period of time.

Whether gallstone formation is preceded by infection, or whether it follows it, and what the significance is of mechanical irritation and obstruction in the process of cholangitis are questions we hope to be able to answer more satisfactorily in the future. The unequivocal facts at the present time are that in any large series of patients over 50 years of age, with clinical histories indicating gallbladder disease of many years duration, a demonstrable impairment of liver function is frequently found. A number of the patients in such a group will also prove to have critically diminished liver function if the burden of an operative procedure is placed upon them.

It is our contention that this process is set in motion at the time the gallstones are forming or shortly thereafter, subsequent to which its course may vary greatly. In some patients, the manifestations of biliary tract disease may be so severe as to be unbearable and surgical treatment is sought. We believe that cholecystectomy performed for cholecystitis with cholelithiasis, if done early in

TABLE IV

CHOLEDOCHOTOMY IN ACUTE CHOLECYSTITIS

The New York Hospital
September 1, 1932 to September 1, 1950
(18 years)

Operative Findings	Patients Under 50	Patients 50 & Over	Total Cases
Stones recovered	19	21	40
No stones found	12	10	22
Total cases	31	31	62

the history of the disease, will lessen the possibility of further liver damage. In other cases, symptoms may be minimal so that the patient learns to tolerate them easily. In still other instances, the symptoms may be entirely absent. Under such circumstances, cholangitis may be the cause of severe liver damage over the years. These patients are said to have "silent" or "reasonably quiet" gallstones. We believe that such stones are an important cause of liver damage and should therefore be removed when diagnosed, unless there is some contraindication to surgery.

CARCINOMA OF THE GALLBLADDER AND EXTRAHEPATIC BILE DUCTS

In 1931 Evarts Graham[5] stressed the point that sufficient attention had not been given to the problems of carcinoma of the gallbladder and extrahepatic bile ducts. This is still true of the present day literature on this subject. According to Kirshbaum and his group[6], carcinoma in these two locations comprises about 6.5 per cent of all cancer, with gallbladder carcinoma at 3 per cent and that for the extrahepatic bile ducts at 3.5. In women, the incidence of nonmalignant disease of the gallbladder is almost four times that in men. Carcinoma of the gallbladder constitutes 8 to 10 per cent of all malignancies found in women. Carcinoma of the gallbladder and extrahepatic bile ducts occurs most frequently in the older

group, although it has been seen as early as 30 years of age. Each decade after 30 shows a definite increase in this condition, but because of the present day distribution in the age groups, the greatest number of cases are found in the range from 50 to 70 years.

Carcinoma of the gallbladder and extrahepatic bile ducts offers a particularly gloomy outlook. A review of the reports on followed cases shows an average of less than a year of life expectancy after diagnosis has been established. Carcinoma of the gallbladder shows an average survival of about one year, whereas carcinoma of the extrahepatic bile ducts is estimated at less than six months. In most instances diagnosis is established only at operation, and in a remarkably high percentage of cases it is an unexpected finding. In an excellent review of the subject, Mohardt[7] states that gallstones are found in more than 80 per cent of the patients with extrahepatic biliary tract cancer. Several writers on this subject believe that between 4 and 10 per cent of all patients with gallstones eventually develop carcinoma of the gallbladder.

Treatment of carcinoma of the gallbladder and extrahepatic bile ducts consists in removing the primary lesion when feasible and the adjacent structures and lymph glands insofar as this can be accomplished. The diagnosis of carcinoma of the gallbladder is ordinarily confirmed only when examined by the surgical pathologist. Although it customarily appears as a well circumscribed lesion, it is invariably followed by widespread metastasis in a matter of a few months. Removal of the liver adjacent to the gallbladder bed by electrical unit and cautery has, in our hands as well as others, also been followed by further tumor spread. True, there are case reports[8,9] of patients surviving from 10 to 15 years, but they are rare. Carcinoma of the extrahepatic bile ducts is usually diagnosed in a late phase of malignancy when extension of the tumor has produced such symptoms as jaundice and weight loss. Perhaps carcinoma of the ampulla of Vater is an exception, since it may produce obstructive jaundice before extension of the tumor takes place. Radical resection, using a Whipple-type of procedure, on this group of tumors has been followed by five year survivals, but there are also reports of equally long survivals following local excision of a tumor and implantation of pancreatic and common bile ducts into the duodenum.

The relationship between gallstones and carcinoma of the extrahepatic biliary tract is not established, but several factors are recognized. First is mechanical irritation from the stones. Second is the associated metabolic changes that accompany gallstones. A third factor, and one that has received consideration more recently, is the possible role of the carcinogens, cholanthrene and methylcholanthrene, which are both related to deoxycholic acid of the bile.

At the present time, the surgical treatment of carcinoma of the biliary tract is by and large ineffectual, but no other form of therapy offers more. Therefore, the greatest hope for control of this disease lies in its prevention. If, as reported in many case series, more than 80 per cent of all carcinomas of the biliary tract occur in patients with biliary lithiasis, and if 4 to 10 per cent of patients with stones develop carcinoma of the biliary tract if they live to 75[7], then it follows

that a policy which stresses removal of the gallbladder containing stones as soon as diagnosis is established should materially reduce the incidence of carcinoma of the extrahepatic biliary system.

Incidental Gallstones

Due to the large number of routine health examinations carried out nowadays, and the increase in the older age groups of the population, the problem of discovering a gallstone on routine examination is frequently encountered. Reviewing the clinical history of these patients often brings to light the fact that they have had symptoms and episodes of a relatively severe nature for many years. When such a history is established, there seems to be little question in anyone's mind that cholecystectomy is the proper procedure to follow. If, on the other hand, there are no current symptoms present and the patient cannot recall any past episodes, then there is a wide difference of opinion between internists and surgeons as to what should be done. Some adhere to the practice advocated at the turn of the century, as stated by Kehr[10] in 1901, that "quiet lying gallstones are no subject for treatment, for a persistent latent stage is almost as good as a cure". Comfort, Gray and Wilson[11] of the Mayo Clinic reviewed this problem in 1948 and reported on 112 cases of "silent gallstones" that were followed for a period of 10 to 20 years. They found that 61 of their cases never developed any symptoms. Thirty of the remaining 51 only complained of symptoms labelled as "dyspepsia", and 21 patients experienced painful seizures. Five of the latter also had jaundice. Of the 51 who developed symptoms, 24 underwent operation, of which 3 died postoperatively. There were also 28 other deaths in the total group of 112. Twenty-one of these, so far as could be ascertained, were deaths not referable to the gallbladder or biliary tract. One patient died of carcinoma of the gallbladder, and death followed cholecystectomy in three instances. For the remaining three cases the exact cause of death is not given, but it was believed to be associated with biliary tract disease.

When one realizes that the operative mortality rate from elective cholecystectomy for cholelithiasis is only .5 to one per cent in our best clinics at the present time, the odds would seem to favor removal of a gallbladder containing stones in order to avoid possible complications later. When such complications are allowed to develop, and surgery is then required to correct them, we find that the mortality rate rises to 3 per cent or higher. And this percentage does not include the deaths that are due to liver damage, systemic diseases, or carcinoma of the biliary tract, all of which often follow the course of biliary tract disease.

Summary

Biliary tract disease which includes stones in the gallbladder or bile ducts is best treated by surgery. For most patients, this brings immediate relief of symptoms and effectively interrupts the course of the disease. Complications and sequelae of nonmalignant biliary tract disease can occur at varying intervals after its onset. The greater the lapse of time after onset of the disease, the greater are the number of complications and the more severe they are likely to be. It follows,

therefore, that surgical treatment should be undertaken soon after diagnosis is established. From our experience, we believe that approximately 50 per cent of the patients can be accurately diagnosed as having acute cholecystitis in the early stages of the disease. Almost without exception this group comprises young women recently pregnant. Cholecystectomy for early acute cholecystitis and cholelithiasis brings relief of symptoms and rapid return to normal activity with negligible risk. Furthermore, it will, to a large extent, prevent the development of the complications that are associated with acute cholecystitis, such as perforation followed by local or generalized peritonitis, or the late phases of biliary tract disease, such as an infected gallbladder containing stones, choledocholithiasis, and associated liver damage. The presence of stones in the gallbladder is indicative of biliary tract disease. The stones may be "silent" and as yet cause no symptoms, but they are not innocent. The same is true of minimal symptoms. Chronic indigestion, for example, may be well tolerated, but such allows the course of the disease to progress. These patients are also prone to liver damage and may even develop acute suppurative or obstructive processes that can only be relieved by surgery under less favorable conditions. If these people live to present day expectancy untreated, 4 to 7 per cent of them may also develop carcinoma.

Conclusions

1. Nonmalignant disease of the biliary tract commonly begins in early adult life, although it is found from infancy to old age.

2. Many patients, perhaps 50 per cent, are subject to attacks of acute cholecystitis in the early phase of biliary tract disease.

3. For patients under 40 years of age, the surgical treatment of acute cholecystitis may be accomplished with minimum risk.

4. The common sequelae and complications of cholecystitis with cholelithiasis include common duct stone, liver damage, carcinoma of the biliary tract, and changes associated with the cardiovascular system.

5. The most effective method now available to prevent these complications or sequelae from following cholecystitis with cholelithiasis is cholecystectomy.

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Discussion

Dr. O. H. Wangensteen:—I suspect that the greater interest in this discussion will perhaps come in Dr. Snapper's field. Now that you have called on me, I will say a few words:

The fundamental problem, of course, is what causes gallstones, and we know very little about that. Dr. Weiser, who just died at the Rice Institute in Texas, who was a physical chemist essentially, I think, did some very interesting studies on cholesterin formations, employing gelatin and silver nitrate to study the penetration of the silver nitrate in the gelatin ring. The crystalloids and colloids have something to do with this.

John Berg, the well-known Swedish surgeon of an earlier generation in Stockholm, spoke of stasis as the cause of stone formation in the gallbladder. Many years ago, I put human gallstones into the dog's gallbladder and noted that they dissolved and disappeared. I suppose the content of bile salt in the bile has something to do with this. In the human, unlike the dog, the bile salt is largely glycocholic bile salt whereas in the dog the bile salt is largely taurocholic acid. I worked at this problem twenty-five years ago; however I realized my shortcomings as a biochemist, so I gave the problem up, and began to explore the more mechanical problem of bowel obstruction, which is more along the understanding and comprehension of a surgeon.

I did notice that a way to get a calculus to form in the dog's gallbladder was to place a bit of cotton together with an attenuated agar culture of streptococci into the dog's gallbladder. This technic succeeded in the production of "gallstones" in the dog's gallbladder.

The recital by Dr. Rehfuss of conditions which may favor the occurrence of gallstones, is reminiscent of all the miasmas which one suspicioned as causing tuberculosis until the tubercle bacillus was discovered. I am reminded of the biostatistician who had a great flair for experimentation; he had been a teetotaler for long years and then with scientific curiosity he undertook to drink successively bourbon and soda; scotch and soda; gin and soda, and finally rum and soda; and each time he got drunk—a circumstance which led him to the conclusion that soda is intoxicating. I suspect here too that, a mere re-enumeration of conditions with which gallstones may be associated may not actually give us much information concerning the etiology of gallstones.

The fundamental factor would appear to be stasis in the gallbladder and the physical chemistry of situations which bring about precipitation in the bile; the problem is essentially one in physical chemistry.

Dr. Snapper, of course, has lived all around the four corners of this terrestrial sphere of ours, and he probably can tell us something about geographic conditions which seem to bear on gallstone formation.

I had the good fortune to be in the West Indies some years ago and they told me that gallstones was one of the common surgical diseases. In any case gallstone formations there seemed to be a more frequent surgical disease than it is here.

With reference to fat ingestion, I should like to make one comment. There was published earlier last year in *Gastroenterology*, an interesting study from the Charity Hospital in New Orleans relating to the point under discussion. It was stated as I remember it that, approximately 48 per cent of hospital admissions were white and 52 per cent of patients admitted were colored. The pathologist making the report recounted the autopsies in which gallstones were present. Of the total number of patients observed with gallstones at autopsy, 77 per cent occurred amongst the white patients. Inasmuch as only 23 per cent of the total number of patients having gallstones were colored, the author rationalized—and one has to admit it is speculation—that the striking difference in the observed incidence of gallstones was because of the larger fat content of the diet of the colored man, such that the colored man's gallbladder empties better.

Well, we do know, of course, following the work of Boyden, that fat empties the gallbladder; this fact is implemented every day in the Graham-Cole test of cholecystography. Yet, we know too that, the incidence of gallstones amongst obese people is far greater than amongst thin people.

As a surgeon, I should like to say something further. I certainly agree with Dr. Rehfuss that the surgeon feels better over the excision of the stone-containing gallbladder than he does over the excision of the so-called "nonfunctioning" gallbladder. In other words, I do not believe that surgeons should go all out for excision of the gallbladder which fails to fill during cholecystography. If he does, both he and his patients are doomed to many disappointments.

With reference to the surgical situation, Dr. Frank Glenn has reviewed the situation so well that I would hesitate to say any more upon the subject. Whether one should excise the symptomless stone-containing gallbladder, which is found accidentally, or just watch it along, is one of those philosophic considerations that Professor Snapper talked about this morning. I don't know how he would feel about this. I go along, in the main, with the conservative group. I do not urge excision of the gallbladder unless the patient appears to have some symptoms. Yet when I am doing a gastrectomy or colectomy and find gallstones present, I invariably excise the gallbladder.

Of course, if you are a cancerologist, you have to think, as Dr. Frank Glenn does, of a casual relationship between gallstones and cancer of the gallbladder. This morning Dr. Snapper went so far as to say that he would not ordinarily advise excision of a leiomyoma of the esophagus. He must have been thinking of the old days when the surgeon could not excise a good segment of the esophagus without great risk. Perhaps some surgeons would say with reference to the cancer problem: Take out the leiomyoma and let's forget about the silent gallstone for the moment.

Dr. I. Snapper:—It is certain that in areas where cholesterol and fat intake are low, gallstones are uncommon and carcinoma of the gallbladder a rarity. For the etiology of carcinoma of the gallbladder, gallstones play a very important, in fact, an all-important role. As a general rule it can be said that men with gallstones must always be operated upon, because their complaints usually persist

notwithstanding diet and medication. In women the latter conservative measures are often more successful—at least temporarily. In all frankness I must confess that many women whom I "treated" conservatively many years ago, as Dr. Rehfuss has indicated, now return with carcinoma of the gallbladder, empyema of the gallbladder, completely obstructed common duct, etc. Thus, in general it can be agreed that anyone who has digestive complaints and visible gallstones or a non-functioning gallbladder has to be operated upon.

As to whether gallstones which don't cause complaints, that is, have not led to cholecystitis have to be operated on, is a different question which has to be decided in each case on its individual merits.

Complaints due to spasm of the sphincter of Oddi have been popular for many years but have been less heard of for the last decade.

Fixation of a glass cannula into a duct in which the pressure is very low, changes the function of the organ due to back pressure. The fact that the gallbladder doesn't act according to Hoyle if a glass tube is tied into the common duct, may not be too significant.

SURGICAL THERAPY FOR GASTROINTESTINAL HEMORRHAGE IN PORTAL HYPERTENSION*

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Introduction

The abrupt onset of severe hematemesis from whatever cause is always a matter of grave concern to internist or surgeon. If the severity of the bleeding comes under the caption of massive hematemesis prompt action is imperative to prevent fatal blood loss.

The rather widespread interest in this problem of upper intestinal bleeding is due to its frequency and gravity[1,2]. This interest is manifest in the large number

Fig. 1—X-ray demonstrating calcified splenic artery aneurysm.

of articles appearing in the current literature and also the importance it attains at local and national meetings.

A perusal of the program of this association will point up this statement, in that three other papers have already been presented, dealing with forms of gastrointestinal hemorrhage in peptic ulcer. The seriousness of bleeding in portal hypertension is also well recognized. Once hematemesis has become clinically

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manifest it will, if unchecked, result in a fatal outcome in the majority of cases. Snell[3] states "only 20 per cent of patients survive one year after their first hematemesis—the other 80 per cent die".

Pathogenesis of Portal Hypertension and the Evolution of Current Surgical Concepts

Adequate evidence has accumulated over the past fifteen years to finally lay to rest the contentious term of "Banti's Syndrome", for a terminology more expressive of our present day concept of the pathogenesis of the disorder now known as congestive splenomegaly or portal hypertension. During this period, the role of congestion in portal hypertension has been emphasized[4-11], the degree of venous hypertension has been measured[12,13], and it has been shown that portal hypertension develops secondary to a variety of obstructive factors in the portal bed. This

TABLE I

Site and Type of Lesion Producing Portal Hypertension (Congestive Splenomegaly)

I. Intrahepatic block
  A. Cirrhosis of the liver
    1. Laennec cirrhosis
    2. Schistosomal cirrhosis
    3. Biliary cirrhosis
    4. Infectious hepatitis
    5. Toxic cirrhosis
    6. Hemochromatosis with cirrhosis
    7. Cruveilhier—Baumgarten Syndome
  B. Sphincter mechanism in hepatic veins (vasospasm)
II. Extrahepatic block
  A. Chronic thrombosis of vein (hepatic, portal, splenic)
    1. Inflammatory
      a. Cavernous transformation
      b. Endophlebitis
    2. Traumatic
  B. Stenosis of vein (portal)
    Congenital, site of fetal valves
  C. Compression of vein (portal or splenic)
    1. Inflammatory cicatrix (cholangitis, pancreatitis)
    2. Pancreatic cyst
    3. Tumors
    4. Aneurysm of splenic artery

is, of course, a reversal of the hypothesis of Banti. The obstructive factor may be either intrahepatic or extrahepatic[8-11]. The predominant primary intrahepatic obstructive factor is cirrhosis of the liver. Two rare types of intrahepatic block with essentially normal liver parenchyma have recently been described. Moschcowitz[14] has shown that thrombosis of the main branches of the hepatic veins may give rise to the clinical picture of portal hypertension even to bleeding esophageal varices. Recent fundamental work by Thomas and Essex[15,16] purports to demonstrate the so-called "sphincter mechanism" in the hepatic veins. These latter workers postulate that a chronic state of vasospasm at this level may also produce portal hypertension. This mechanism may be present in some cases in which clinically, and at operation, the surgeon finds a normal liver and no grossly discernible block. Portal hypertension may be general, or local. The hypertension is

termed general when it involves the entire portal system. This occurs notably in cirrhosis of the liver or portal vein obstruction. The hypertension is local when it is confined to the splenic vein and its immediate tributaries, to the cardiac end of stomach, and esophagus[8,17]. Our knowledge of the various types of intra- and extrahepatic blocks producing portal hypertension is gradually expanding and as just mentioned new types are being reported as clinician and investigator continue to probe this problem (Table I). With progression of the disease splenic enlargement ensues and with this a selective cytopenia or pancytopenia, or what is now termed "Hypersplenism"[18].

Surgical Therapy

Time limitation precludes an exhaustive discussion of necessary requisites needed to justify a diagnosis of portal hypertension. Our discussion today is limited primarily to the surgical therapy advocated in this disorder. The bleeding, particularly the severer types, probably most frequently occurs from rupture of

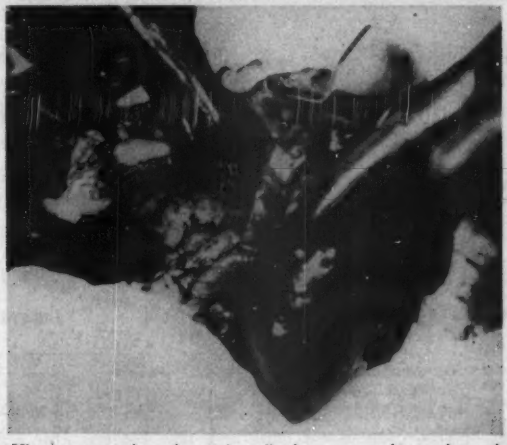

Fig. 2—View at operation of cyst in tail of pancreas obstructing splenic vein.

esophageal varices. However, in our opinion, less severe blood loss may occur from dilated veins in the gastric cardia or even in the small or large intestine due to hypertension in the superior and inferior mesenteric veins as a part of a generalized portal hypertension. In such cases melena, rather than hematemesis, may be observed. A rational surgical approach to this problem must include: 1) The control of the portal hypertension and recurring bleeding, and, 2) the correction of the hypersplenism and its attendant blood changes by splenectomy. Any surgical attack failing to encompass both "desirata" is, in my opinion, irrational. The problem of bleeding esophageal varices is attracting increasing attention by surgeons in several clinics here and abroad. Five different types of operation have now been advocated, attesting to the difficulties inherent in the problem (Table II).

A survey of this list will reveal that in at least one operation—periesophageal packing—not only is splenectomy not performed, but the peritoneal cavity is not

entered. It follows that in this type of operation neither the exact diagnosis nor the mechanism of the portal block can be ascertained. From Table I, we see, and as will be demonstrated later, certain easily remediable lesions may block the splenic vein close to splenic hilum. Abdominal exploration, therefore, with venous pressure readings and tissue biopsy (liver, lymph node, spleen) must be a basic part of any operation proposed.

TABLE II

Operative Procedures Advocated in Portal Hypertension (Congestive Splenomegaly) for Control of Hemorrhage from Esophageal Varices

A. Direct venous anastomosis between portal and caval systems
   1. Portacaval shunt[19,20]
   2. Splenorenal shunt with splenectomy[10,21,22,23]
B. Esophagogastrectomy[24,25]
C. Mediastinal (periesophageal packing)[26]
D. Devascularization of lower esophagus and cardia; splenectomy; vagotomy; gastroenterostomy[27]
E. Total gastrectomy[24,28]

The other procedures listed in Table II are of recent origin, still in the proving stage, and further comment is premature at this time.

The surgical treatment advocated and practiced in our clinic may be summarized in this way: After a clinical diagnosis is made and if no contraindications are discovered, the patient is prepared for surgery. A thoracoabdominal approach is routinely used[10,29,30], and through the abdominal component of the incision, the

TABLE III

Cases With Combined Splenectomy and Splenorenal Shunt

Case	Sex	Age	Obstructive Factor	*Operative Mortality	Late Mortality
1	M	40	Not demonstrable (normal liver)		—
2	F	58	Laennec's Cirrhosis		17 mos. Cholemia, hematemesis.
3	F	54	" "		—
4	F	54	" "		—
5	M	43	" "		—
6	M	54	" "	No Operative	2 mos. Hematemesis.
7	F	55	" "	Mortality	2 mos. Cerebrovascular accident.
8	F	64	" "		—
9	F	19	" "		—
10	M	49	" "		—
11	M	36	Posthepatitis Cirrhosis		—
12	M	52	Laennec's Cirrhosis		—
13	M	53	" "		—

*Denotes entire hospital stay.

diagnosis is confirmed, or disproved, before the thorax is entered. At this time, the surgeon can usually determine with certainty the nature and location of the obstructive factor and whether the patient has a general portal hypertension as occurs in cirrhosis, or a localized splenic vein hypertension. If the former situation is discovered, then a combined splenectomy and venous shunt is our practice. The type of shunt uniformly employed in this series was an anastomosis *by suture*,

end of splenic vein to side of left renal vein (a splenorenal shunt). During the anastomosis only the splenic circulation is temporarily occluded. The renal circulation is intact throughout the course of the vein suture and, of course, the kidney is preserved[10]. If a splenic vein stenosis is found close to splenic hilum, splenectomy alone (without a venous shunt) and, where feasible, excision of the obstructive lesion, will suffice (Figs. 1, 2, 3 and 4). These pictures illustrate types of obstructive lesions encountered in cases 15, 16 and 17 of the subsequent series.

The clinical experience which will now be presented in some detail includes a group of *17 patients, all of whom were operated upon by the author, during the past two years at St. Vincent's Hospital, New York City.

Fig. 3—Excised spleen with attached hilar structures. Note intimate attachment of pancreatic tail and included pancreatic cyst.

The cases are divided into two categories—those requiring combined splenectomy with a splenorenal shunt, i.e., patients with general portal hypertension, and those necessitating splenectomy without a shunt but usually with removal of a specific lesion as just portrayed, i.e., patients with local splenic vein hypertension.

In this first grouping (Table III), 13 consecutive cases were subjected to the same surgical operation, i.e., combined splenectomy and splenorenal shunt. All but two patients were above the fifth decade in the life span. Twelve cases had proven cirrhosis, 11 of the Laennec type, and one patient had a posthepatitis cirrhosis—a sequel to yellow fever vaccine.

It will be noted that there was no operative mortality in these 13 consecutive shunt cases, and although this series is exceedingly small, it represents an im-

*One case, #11, was operated upon by the author at the Veterans Administration Hospital, Bronx, N. Y., courtesy of Dr. P. K. Sauer.

provement over a 21.4 per cent operative mortality reported by the author in an earlier series some two years ago.

The three late fatalities in this group will be discussed in a subsequent section of the paper.

The next table (Table IV), details four cases in which splenectomy alone was performed. In two instances excision of a calcific aneurysmal mass, and in one instance excision of a pancreatic cyst, was done at the time of the splenectomy. (Figs. 1, 2, 3 and 4.) Here again there was no operative mortality and, at this reporting, no late mortality.

Recurring exsanguinating bleeding was the dominant feature in 14 of the 17 patients, i.e., in 10 of the 13 shunt series and all four of the non-shunt series. Massive hemorrhage was the direct cause of an emergency hospital admission in most instances. Three patients never showed clinical bleeding but gave x-ray

Fig. 4—Same as Fig. 3, with cyst sectioned to show its interior. An accessory spleen may be seen at the lower right margin.

evidence of varices, plus the clinical signs of hypersplenism, and these were the determining factors in electing surgery. One of these cases proved to be an extremely rare type of portal hypertension, known as Cruveilhier-Baumgarten Syndrome[31]. In this bizarre condition, clinical requisites for diagnosis include: an abdominal thrill and bruit over a functioning fetal umbilical vein, cirrhosis, esophageal varices and hypersplenism. This case, (#8), is to be separately published and is, I believe, the first of its kind to be operated upon and submitted to combined splenectomy and splenorenal shunt. Figure 5 is a schematic drawing depicting the relation of the fetal umbilical vein to the fetal portal circulation. Normally, this vein is spontaneously obliterated at, or shortly after, birth. Figure 6 graphically displays the greatly dilated umbilical vein in our patient at operation. It is seen extending from abdominal wall to upper surface of liver. It is over this point that the thrill and bruit are easily detected, on the abdominal wall (Fig. 7).

Three patients (#2, 4, 7) besides having varices and no gross bleeding before operation, did have associated severe ascites for at least 12 months prior to surgery.

TABLE IV

CASES WITH SPLENECTOMY ALONE
(NO SHUNTING PROCEDURE)

Case	Sex	Age	Obstructive Factor	*Operative Mortality	Late Mortality
14	M	11	Thrombosis or cavernomatous transformation of splenic vein	No Operative Mortality	No Late Mortality
15	F	49	Calcified aneurysm of splenic artery		
16	M	44	" "		
17	F	25	Cyst of tail of pancreas		

*Denotes entire hospital stay.

RESULTS

Information on the late results in the entire series may be readily obtained by reference to Table V.

TABLE V

FOLLOW-UP RESULTS

	Case	Type of Surgical Procedure	Months Followed After Operation	Results
Venous Shunt Cases	1	Splenectomy and Splenorenal Shunt	24	Excellent
	2		17	Death; Cholemia, Hematemesis
	3		21	Excellent
	4		18	Excellent
	5		16	Excellent
	6		2	Death; Hematemesis
	7		2	Death; Cerebrovascular Accident
	8		8	Excellent
	9		8	Excellent
	10		5	Excellent
	11		3	Excellent
	12		1	Excellent
	13		1	Excellent
Non-Shunt Cases	14	Splenectomy	14	Unimproved; Recurring Hematemeses
	15	Splenectomy and Excision of Calcified Splenic Artery Aneurysm	19	Excellent
	16	Splenectomy and Excision of Calcified Splenic Artery Aneurysm	8	Excellent
	17	Splenectomy and Excision of Pancreatic Cyst	3	Excellent

Of the 13 cases in the venous shunt group, all but three have survived and have been well and entirely free of further bleeding for periods up to two years. The blood picture in the 10 cases with "excellent" results has remained normal

for the periods given. The three deaths occurred in cases 2, 6, 7 and took place 17, 2 and 2 months, respectively, after operation. Cases 2 and 6 are definite failures, as proven by postmortem, with atresia and stenosis, respectively, of the venous anastomosis. Liver failure also was a major factor along with hematemesis as part of the terminal picture in Case 2. Case #7 was readmitted to the hospital because of a sudden hemiplegia two months after the initial hospitalization. Her dominant preoperative sign had been recurring ascites. The ascites did not recur during the short span before death. Unfortunately, no autopsy was obtained in this instance. Our late mortality in the shunt group is 3 out of 13, or 23 per cent.

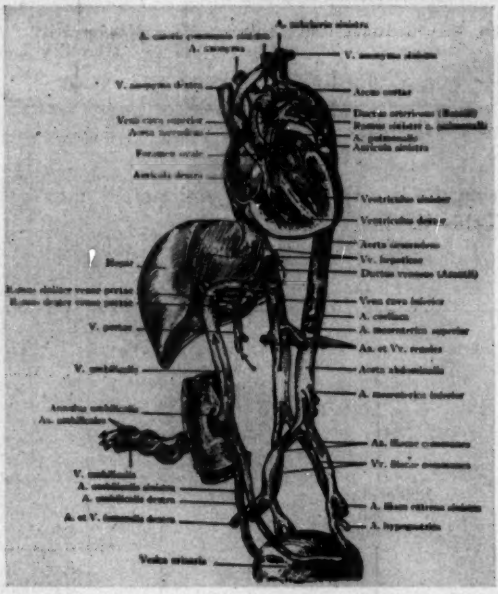

Fig. 5—Diagram of the fetal circulation about the time of birth. Note course and position of umbilical vein as it enters portal system. (From Callander's "Surgical Anatomy", 1933, W. B. Saunders Co.)

A perusal of the second group on Table V of only four cases in the non-shunt group shows no late deaths. All these patients, as you will recall, had severe bleeding before operation. Three have been completely relieved of this dread symptom and are entirely well for 19, 8 and 3 months, respectively. The single unimproved case is a failure, and undoubtedly has obstruction of the portal vein in addition to splenic vein. This was not demonstrable at operation. There is a strong likelihood that in this 11-year old boy we are probably dealing with a congenital cavernomatous transformation of both portal and splenic veins[32]. This patient is being readied for a secondary procedure in the near future.

The operative mortality in the entire series was, therefore, zero. The late mortality in the shunt group with an intrahepatic block was 23 per cent.

Comparing these figures with those reported over two years ago[21], there is a marked drop in hospital mortality from 21.4 per cent to zero, and from 12.5 per cent to zero in each group, respectively. The late mortality likewise shows improvement with a decline from 38 per cent to 23 per cent in the group with an intrahepatic block. The non-shunt group, albeit very small, has shown no late mortality at this writing.

Summary

1. Gastrointestinal hemorrhage in portal hypertension is a serious symptom. When enteric bleeding has once become clinically manifest, it will, if unchecked, result in a fatal outcome in the majority of cases.

Fig. 6—Greatly dilated umbilical vein coursing from abdominal wall to upper surface of cirrhotic liver between right and left lobes.

2. Two unusual types of intrahepatic block are described—hepatic vein thrombosis, and chronic vasospasm of the "sphincter mechanism" in the hepatic veins. These lesions may produce portal hypertension and esophageal bleeding. Such cases are confusing to the surgeon because the liver appears grossly normal and the basic lesion is not demonstrable at laparotomy.

3. A rational surgical approach to the problem considered in this paper must include two desirata—(1) The control of portal hypertension and recurring bleed-

ing, and, (2) the correction of the hypersplenism and its attendant blood changes by splenectomy. In an attempt to achieve this, the author advocates combined splenectomy and splenorenal shunt, or splenectomy alone for splenic vein obstruction. Local extirpation of the obstructive lesion is performed when indicated.

4. Other operative procedures are sponsored by certain students of this problem.

5. In a comparatively small series of 13 consecutive splenorenal shunts, no operative fatalities occurred. Twelve of these cases had advanced cirrhosis of the

Fig. 7—Abdominal infra-red photograph (Case No. 8) showing site on abdominal wall of thrill and bruit arising from underlying umbilical vein.

liver. This represents a decline from a previously reported 21.4 per cent mortality rate. A late mortality of 23 per cent occurred in cases followed from 1 to 24 months. The survival group have all been well and have had no recurrence (for the periods stated) of the preoperative symptoms (9 hematemesis, 1 ascites).

6. In the four cases with splenectomy alone there was no operative and no late mortality for the periods stated. Three of these have had no further bleeding.

7. A case of Cruveilhier-Baumgarten syndrome is included in this series. It is believed to be the first case reported in the literature in which a successful splenorenal shunt has been accomplished.

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Discussion

Dr. O. H. Wangensteen:—I hesitate to intrude myself upon your time on the program; it is running a little behind. I do want to take this occasion to compliment the previous speaker on a very excellent presentation. He omitted to say that, he himself had a lot to do with the demonstration of this syndrome of portal hypertension.

It is an interesting disease. I visited in Florence, Italy, long years ago and walked outside one of the hospitals there and saw the name of Banti on a little stone in the sidewalk in front of the hospital. My recollection of that circumstance now reawakens many memories in me, as it would have done in any of you.

I think all of us, following the work Dr. Rousselot has done, are convinced he has made a major contribution to our understanding of a very difficult syndrome. My associate, Dr. Baronofsky and I, have worked at it in a little different way. For long years we investigated the abetting factors in ulcer and, as you can understand, anemia of the mucous membrane is an abetting factor.

Eppinger said about 20 per cent of patients died of hemorrhage in cirrhosis of the liver. As many of you know, Baronofsky and I have studied abettment of the ulcer diathesis in portal hypertension. It is real. In 1945 I wrote a paper on gastric resection for occult alimentary tract bleeding with hematemesis (Lister Lecture, *Canad. M. A. J.* **53**:309, 1945).

I also reported having done a 95 per cent excision of the stomach, and in another patient a 98 per cent gastrectomy for the bleeding of portal hypertension. Shortly thereafter when we had learned to do total gastrectomy with a lesser operative mortality, I did total gastrectomy for the bleeding of the hematemesis resulting from the portal hypertension of the Banti syndrome. Later, when I took to the sleeve resection for ulcer, I excised the entire acid secreting area, allowing the antrum to remain. The esophagus is then anastomosed to the antrum. Because of the coincidental vagotomy on the antral fragment, it is necessary to do a simultaneous pyloroplasty to insure proximal gastric emptying.

I believe, as the author stated, a double-ended attack on this disease is smart; you will remember he said two of his patients died subsequently of gastric hemorrhage; one admittedly had cholemia from failure of liver function.

Everyone who has operated upon patients with cirrhosis has had occasion to reflect on how poorly they withstand operation. I would like to ask Dr. Rousselot whether he selected his patients for operation in any way? Do the internists select the cases? Are cases of poor liver function ruled out? Nevertheless, does diminishing the portal pressure improve liver function such that death from cirrhosis or liver failure is postponed? Are not all patients with liver cirrhosis going to die of liver failure anyway? One must not of course minimize the worthwhileness of palliative procedure.

I would like to ask Dr. Rousselot to prophesy, if he is willing to affect even the role of a minor prophet, as to whether his patients who have cirrhosis are going to be cured by the operation he has done for portal hypertension.

Dr. Louis M. Rousselot:—I refuse to assume the role of a prophet, but would be willing to prophesy to this extent, that undoubtedly a number of these cirrhotics will die of their cirrhosis and not of their hematemesis. I think in the long-term follow-ups, over two years, if they haven't had recurring hematemesis, the chances are that their remaining threat is the hepatic damage, and, whatever the initiating factor in that disease is, is still in operation. We do not think we have overcome it.

Dr. Wangensteen:—Did the two patients who died of gastric hemorrhage have a thrombosis at the site of the anastomosis?

Dr. Rousselot:—They obliterated their anastomoses. We tried at the time of operation to make little notes, just as you do, on your golf score, for instance, of how you could have improved that particular hole, and it is of interest that we noted in these two that these were two operations which we felt technically left a lot to be desired.

Dr. I. Snapper:—As a partial answer to Dr. Wangensteen, I am not only impressed by the fact that after operation his patients do not have a tendency to hemorrhage anymore, but that they also show improvement of liver function.

I do not completely see eye to eye with him about the so-called Cruveilhier-Baumgarten syndrome. If the presence of a venous hum, (not a bruit!) comparable to the sound heard when a shell is placed against the ear, would prove the presence of a Cruveilhier-Baumgarten syndrome, then practically every liver cirrhosis patient in the Orient would suffer from that syndrome. The formation of murmurs and hums depends very much upon physical qualities of the blood. Just as in anemia, a venous hum is heard over the jugular vein, in patients with liver cirrhosis and anemia and hypoproteinemia venous hums are heard over the collaterals which connect the portal circulation with the cava circulation, that is, in the neighborhood of the umbilicus. Therefore, it is not justified to diagnose a Cruveilhier-Baumgarten's syndrome in all cases where venous hums can be found.

I gladly agree that the surgeons have certainly opened up a new future by the shunt operation for the bleeding cirrhosis patients.

Dr. Rousselot:—I remember only one question, on the matter of selection. The matter of selection was entirely one of whether the patient at the time of operation had a reasonably compensated liver; in other words, protein, Hanger's test—we have done many with a Hanger's test, the two-plus and four-plus level, a general clinical assaying of the patient's condition, but, by and large, we are very anxious to do every case of the hemorrhage group and have. We think we have not missed any. They are usually the patients who refuse operation.

KOLANTYL, A NEW ANTISPASMODIC PREPARATION FOR COMBINED THERAPY OF PEPTIC ULCER

A Preliminary Report

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Kolantyl is a recently developed compound whose active ingredient is the new antispasmodic, Bentyl Hydrochloride*. In tablet form for oral administration, Kolantyl provides an improved method of therapy for peptic ulcer and other disorders accompanied by smooth muscle spasm, through the synergistic action of its various components.

The spasmolytic effectiveness of Bentyl Hydrochloride was first demonstrated in a small series of patients, most of whom had failed to respond to atropine and the older synthetic substitutes[1]. Similarly favorable results have now been obtained in 67 patients suffering from a variety of gastrointestinal disorders or from primary dysmenorrhea. Symptoms were relieved to a highly gratifying extent by the administration of Bentyl Hydrochloride, as outlined in Table I. The value of this new antispasmodic and the relatively low incidence of its side effects have been confirmed by other investigators[2,3]. In cases of gastric or duodenal ulcer, however, it was frequently noted that the symptoms were only partially relieved. This observation has also been reported by others working with atropine and dibutoline (Merck) by injection[4].

In an attempt to improve the response of ulcer cases, we administered Bentyl Hydrochloride orally in combination with antacids (magnesium oxide, hydrated aluminum oxide) and methylcellulose. This combined therapy gave encouraging results as measured by relief of symptoms and roentgen evidence of improvement. As a result, a study was undertaken to evaluate synergistic therapy with a tablet made according to the following formula, and given the name Kolantyl†.

Bentyl Hydrochloride	5 mg.
Aluminum Hydroxide Gel	400 mg.
Magnesium Oxide	200 mg.
Sodium Lauryl Sulfate	25 mg.
Methylcellulose	100 mg.

The various ingredients of this compound, acting synergistically, are designed to produce optimal results in cases of peptic ulcer. Singly, the components of Kolantyl may be expected to possess the following types of activity:

1. Antispasmodic:—The antispasmodic agent, Bentyl Hydrochloride, has been shown to exert both a parasympathetic depressant and a musculotropic action upon the smooth muscles of the gastrointestinal tract and to have little or no my-

*Bentyl Hydrochloride is a trade-mark of The Wm. S. Merrell Company, of Cincinnati, Ohio, for its brand of dicyclomine hydrochloride (diethylaminocarbethoxybicyc.ohexyl hydrochloride). The material was kindly supplied by the Clinical Research Department of that firm.

†Kolantyl is the trade-mark of The Wm. S. Merrell Company, of Cincinnati, Ohio, for this preparation.

driatic effect or drying effect on the salivary secretions[1,2,3,5]. The usual dose is 10 mg. (given three times a day). On a milligram basis this dose should be several times as potent as the usual dose of atropine, but not sufficient to produce the undesirable side effects commonly associated with atropine[5].

2. *Antacid:*—The anticholinergic activity of Bentyl Hydrochloride may contribute to the reduction of acidity provided by magnesium oxide which acts quickly, and aluminum hydroxide which has an intermediate period of action. Neutralization of acid by these agents is illustrated in Figure 1*.

3. *Demulcent:*—By reason of its content of methylcellulose, the synergistic compound should form a protective coating over the ulcerated mucosa of the stomach and duodenum and prevent irritation of the lesions by the action of acid and

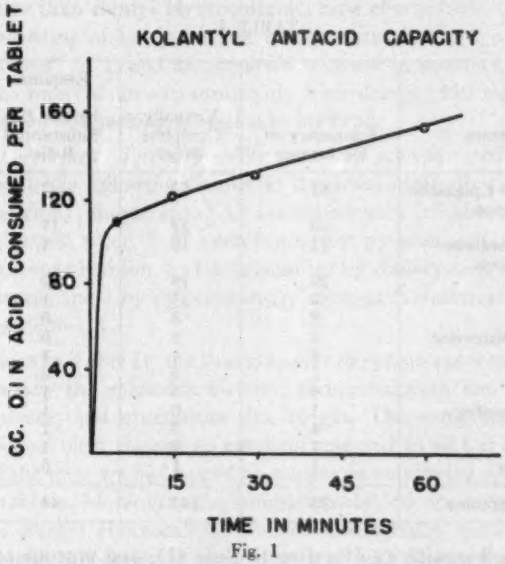

Fig. 1

digestive enzymes. Methylcellulose may also be expected to hold the active ingredient in the ulcerated areas. This substance has been shown to have a demulcent action on the gastrointestinal mucosa[6].

4. *Antilysozyme Activity:*—It is believed that lysozyme as well as pepsin and hydrochloric acid is a probable etiologic agent in the pathogenesis of peptic ulcer, although its exact role is still controversial[7-13]. It seems to be well established, however, that sodium lauryl sulfate alone or sodium alkyl sulfate (a mixture of sodium lauryl, palmityl, stearyl, and oleyl sulfates) is capable of inhibiting the lysozyme and peptic activity of the gastric juice without changing its pH[14-19]. Fogel-

*Data kindly supplied by the Scientific Division of The Wm. S. Merrell Company, Cincinnati, Ohio.

son and Shoch[19] used these detergent agents alone to treat 34 patients suffering from gastroduodenal ulcerative disease, which had resisted all orthodox methods of therapy, and obtained relief of symptoms in 26, who recovered sufficiently to return to their normal activities. It seems likely that lysozyme activity is only one of many factors in the production of peptic ulcer and that adequate therapy should be aimed at the control of as many factors as possible.

Results of Treatment With Bentyl and Kolantyl

Bentyl Therapy Alone:—Following the encouraging results we obtained from Bentyl in our preliminary study[1], the drug was used in 67 patients ranging in age from 17 to 76, who were suffering variously from the irritable spastic colon syndrome (30), duodenal ulcer (17), primary dysmenorrhea (10), cholecystitis and biliary dyskinesia (6), pylorospasm (6), psychoneurosis (3), duodenitis (3), gastric ulcer (3), food sensitivity (1), diverticulitis (1), and mucous colitis (1). Table I lists 195 symptoms accompanying these disorders, 147 (75 per cent) of which were relieved by Bentyl Hydrochloride, while 44 (23 per cent) were partially relieved, and only 4 (2 per cent) were unimproved.

TABLE I

Symptoms	Frequency of Occurrence	Response		
		Virtually Complete Relief	Partial But Substantial Relief	Failure
Abdominal or Epigastric Pain or Cramps	61	52	7	2
"Gas"	40	22	17	1
Abdominal Soreness and Tenderness	11	10	1	0
Constipation	29	19	10	0
Nausea	17	15	1	1
Diarrhea	8	8	0	0
Abdominal Distention	6	6	0	0
Backache	8	4	4	0
Eructation	2	2	0	0
Vomiting	6	5	1	0
Epigastric Burning	1	0	1	0
Chest Pain	4	3	1	0
Pyrosis	1	0	1	0
Regurgitation	1	1	0	0
All Symptoms	195	147	44	4

Chamberlin[2] reported good results from Bentyl Hydrochloride in a group of similar disorders. He treated a total of 111 patients for one to three months and was able to evaluate the effects in 71 at the time of his report. Almost complete symptomatic relief was obtained in 36 (over 50 per cent), excellent but incomplete relief in 24 (34 per cent), and little or no benefit in 11 (15 per cent). All but 6 of 62 instances of the irritable colon syndrome responded well, and all but 1 of 7 cases of dysmenorrhea. The 2 cases of peptic ulcer and the 2 of diverticulitis and diverticulosis were not benefited. The usual dosage of Bentyl Hydrochloride was 10 mg.

three times a day, but 14 patients received twice this amount. Side effects were few (6 cases) and mild. Only 1 of the 111 patients treated had a noticable decrease of salivary secretion.

Hock[3] also reported gratifying results from Bentyl Hydrochloride. He treated 67 patients suffering from gastrointestinal disorders, 63 of whom had excellent to complete symptomatic relief, with only 4 not responding (2 of 58 with functional bowel distress, 1 with gastric ulcer, and 1 with cancer). The usual dosage of 10 mg. three times a day was effective in most of the patients, but some required 20 mg. three or four times daily. In 15, concurrent sedation was found to be necessary for optimum results, and for this purpose capsules of Bentyl with phenobarbital proved effective. Most of the patients treated had not been benefited by the older antispasmodics, and in 20 cases belladonna and phenobarbital was tried and found to be less effective than Bentyl Hydrochloride. Side effects from this therapy were insignificant, consisting of headache and vertigo occurring in 2 patients, a feeling of "light-headedness" in 1, and an apparent increase in spastic constipation in 1. One patient who received an extraordinarily high dosage, 130 mg. three times in one day, complained of a jerking sensation in his head.

Kolantyl (Combined) Therapy:—We have now administered Kolantyl tablets to 30 patients with the following disorders: duodenal ulcer, 19 (2 complicated by hypertrophic gastritis); duodenitis, 3 (1 associated with irritable colon and 1 with spastic colon); gastric ulcer, 3 (1 complicated by pylorospasm and 1 by hypertrophic gastritis); spastic colon, 3 (1 accompanied by cholecystitis and hyperacidity, 1 by psychoneurosis, and 1 by pylorospasm); acute gastrointestinal episode, 1; and gastritis with duodenitis, 1.

As will be seen in Table II, the vast majority of symptoms were relieved wholly or in part, especially the epigastric distress, abdominal pain and cramps, and the distention, flatulence, and eructations due to gas. The symptoms accompanying gastric and duodenal ulcer showed an excellent response in all but 2 of the 22 cases. This was one of the ends we had hoped to achieve in employing synergistic therapy with Kolantyl tablets. Moreover, the comparatively low incidence of side effects with the use of Bentyl Hydrochloride, which had already been observed[1,2,3], is especially notable in this series of patients treated with Kolantyl, only one patient showing any untoward reaction.

Three of the cases in Table II are abstracted below as examples of the typical response to Kolantyl therapy:

Case 15:—D.A.D., aged 53. For the last three years this man has experienced dull epigastric pain for two hours after meals. He has been on bland diets and a variety of antacids with some relief, but during the last few months the proprietary antacids have given only slight or no relief. X-rays taken last fall revealed a small gastric ulcer and pylorospasm; gastroscopic examination some months later confirmed the diagnosis of benign gastric ulcer. This patient was placed on an ambulatory ulcer diet and given one Kolantyl tablet six times a day. There was excellent

TABLE II

RESULTS IN 30 PATIENTS TREATED WITH KOLANTYL

Cases	Sex	Age	Diagnosis	Therapy: Dosage (tablets)	Therapy: Duration (days)	Side Effects	Symptomatic Relief of Manifestations of Muscle Spasm Present: Epigastric distress	Abdominal pain	Chest pain	Abdominal cramps	Spastic constipation	Nausea	Vomiting	Gas (distention, bloating, eructation, flatulence)	Regurgitation	Backache	Discomfort after meals	Recurrent obstruction	Localized tenderness	Rigidity	Diarrhea	Headache
1. C.M.	M	58	Duodenal ulcer	2 q.i.d.	100	none	++			++	+			++								
2. A.E.	M	31	Duodenal ulcer early	2 q.i.d.	60	none	++			++	++					++						
3. C.J.W.	M	32	Duodenitis	2 q.i.d.	60	none		++		++	+	++		+								
4. H.L.	M	58	Duodenal ulcer	2 q.i.d.	40	rectal irrit.		+			+	+		—								
5. E.H.	M	36	Duodenal ulcer	2 q.i.d.	76	none		++	++	++	+			++								
6. M.H.	F	62	Gastric ulcer	2 q.i.d.	90	none		++	++					++		+						
7. G.C.	M	49	Duodenal ulcer	2 q.i.d.	30	none	++	++			++			++								
8. T.L.	M	54	Duodenal ulcer	2 q.i.d.	72	none	++				+			++		++						
9. J.F.K.	F	44	Spastic colon; cholecystitis; hyperacidity	2 t.i.d.	30	none				++		++		+	+							
10. J.C.M.	M	35	Duodenitis	2 q.i.d.	52	none		++			+			++	++							
11. H.O.	M	36	Duodenal ulcer	2 q.i.d.	76	none	++			++				+							+	
12. E.N.	F	43	Duodenal ulcer	1-6x daily	100	none		++	+		++		++	++		++						
13. E.J.S.	M	37	Spastic colon; psychoneurosis	1-6x daily	7	none	—							—			—					—
14. J.B.C.	M	46	Duodenal ulcer	1-6x daily	21	none												—				
15. D.A.D.	M	53	Gastric ulcer; pylorospasm	1-6x daily	80	none	++												++			

TABLE II (Continued)

Cases	Sex	Age	Diagnosis	Therapy: Dosage (tablets)	Therapy: Duration (days)	Side Effects	Symptomatic Relief of Manifestations of Muscle Spasm Present: Epigastric distress	Abdominal pain	Chest pain	Abdominal cramps	Spastic constipation	Nausea	Vomiting	Distention, bloating, eructation, flatulence	Regurgitation	Backache	Discomfort after meals	Recurrent obstruction	Localized tenderness	Rigidity	Diarrhea	Headache
16. O.W.M.	F	36	Acute G.I. episode following influenza	1-6x daily	21	none	++							++			++					
17. T.C.	M	36	Duodenal ulcer	1-6x daily	60	none													++	++		
				1 t.i.d.*	—	none																
18. F.V.	M	55	Duodenal ulcer	1-6x daily	30	none																
				1 q.i.d.*	—	none	++												++	++		
19. D.A.	M	25	Duodenal ulcer	2-6x daily	30	none	++										++		++			
20. L.M.	M	52	Duodenal ulcer	1-6x daily*	62	none	++												++			
21. J.W.	M	24	Gastritis; duodenitis	1 q.i.d.*	54	none	++				++			++						++		
22. T.M.	F	30	Duodenal ulcer	1-6x daily	96	none	++					++		++					++			
23. B.C.	M	28	Duodenal ulcer	1-6x daily	112	none													++	++		
24. H.K.	M	55	Spastic irritable colon; pylorospasm	1 t.i.d.*	65	none		++						++			++					
25. W.M.K.	F	19	Gastric ulcer with hypertrophic gastritis	2 q.i.d.	30	none		++			++			+								
26. J.P.	M	27	Duodenitis; spastic colon	2 q.i.d.	64	none		++			++	++	++	++								
27. J.H.	M	35	Duodenal ulcer	2 q.i.d.	30	none	++	+			+						—					
28. J.G.C.	M	49	Duodenal ulcer	2 q.i.d.	30	none	++	++						++	++				++			
29. C.J.M.	M	58	Duodenal ulcer with hypertrophic gastritis	2 t.i.d.	30	none	++	++			+	++	++	+								
30. R.L.	M	27	Duodenal ulcer with hypertrophic gastritis	2 q. 2 hrs.	10	none		+				++	++	+								

*Supplementary therapy (Bentyl, other antacid, diet) given

++ Virtually Complete Relief

\+ Partial Relief

— Little or no Relief

relief of ulcer symptoms in one week, complete relief in less than two weeks, and x-ray evidence of rapid healing of the gastric ulcer in one month.

Case 24:—H.K., aged 55. This man is a high strung, tense, apprehensive business executive, who was suffering from a spastic, irritable colon and pylorospasm. For many years he had experienced abdominal pain, burning sensations, and "gas" shortly after meals, despite the fact that numerous clinical, laboratory, and x-ray examinations were negative. All known antacids, antispasmodics, and sedatives had been used, with variable and sometimes none too satisfactory relief. He was started on Bentyl with phenobarbital before meals, and this gave fairly good results—not complete relief but better than had resulted from previous medication. Later, one Kolantyl tablet one-half hour after meals for heartburn and sour stomach. This combination still later was changed to one Bentyl with phenobarbital capsule before meals and one Kolantyl tablet one-half to one hour after meals. While the Bentyl with phenobarbital seemed slightly more effective than the other commercial antispasmodics in combination with phenobarbital, the synergistic combination provided further relief, but the two combinations of Bentyl with phenobarbital and Kolantyl gave the most satisfactory results.

Case 23:—B.C., aged 28. This man has had recurrent attacks of duodenal ulcer for about four years. He experienced some relief on an ulcer diet plus Gelusil, 8 c.c. six times a day, and tablets of belladonna with phenobarbital before meals, but after one month he continued to have some distress once every day or so. Bentyl with phenobarbital capsules were then substituted, and after two weeks he began to have complete relief. The patient was then switched to Kolantyl, one tablet six times daily without any other medication. This was followed by subjective relief of ulcer distress and disappearance of tenderness and rigidity over the duodenum. Thus it appears that both Bentyl with phenobarbital and Kolantyl proved effective in the treatment of ulcer, relieving spasm, and controlling acidity.

Summary and Conclusions

Combined therapy of gastrointestinal ulcerative and spastic disease with Kolantyl tablets, tried for the first time in a series of 30 patients, has given extremely gratifying results. These tablets contain a new antispasmodic, Bentyl Hydrochloride, together with antacids, a demulcent, and an antilysozyme agent.

Bentyl Hydrochloride alone has been used by the author in two series totaling over 100 cases, and found to be unusually effective and to cause minimal side reactions as compared with atropine and the older synthetic substitutes. Similar observations have been reported by other investigators, who have treated a total of 138 cases with Bentyl Hydrochloride. Most of the cases in all the series reported have proved intractable to the usual methods of treatment.

Synergistic therapy with Kolantyl tablets has shown an improvement over Bentyl Hydrochloride alone in the small number of patients thus far observed, especially in the relief of peptic ulcer. On the basis of these findings, it is believed that further trials of Kolantyl tablets are warranted. They should be used in conjunction with diet, sedation, psychotherapy, and surgery when these are indicated.

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A SYMBOL OBSERVED ON MIGRAINE CASES

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Migraine is one of the commonest conditions encountered in medical practice. It is estimated that 8 to 12 per cent of all patients treated by general practitioners are migrainous. Unfortunately, the problem is complicated in that signs and symptoms can be so varied that diagnosis is most difficult. As a rule the patient will emphasize the accompanying gastrointestinal symptoms but fail to mention the severity of the unilateral headaches from which he suffers. Nausea, vomiting, vertigo, severe fatigue and abdominal distress appear to be the chief complaints. The sufferer may believe that headaches are caused by sinus trouble, nerve strain or ocular fatigue and yet not include headaches as the chief complaint when being interviewed by the physician. Alvarez[1] states: "The diagnosis of migraine can be made only from the history. Tests and roentgenological studies help not at all when, as usually happens, they are negative. When they are positive they are likely to cause only confusion and mistakes because what they reveal are not the cause of the symptoms."

In my effort to simplify the problem of diagnosing migraine I have tried to observe a common sign in most of these patients. Within a three year period I was able to observe one which might be established as being typical. It is located on the forehead and was observed in more than 88 per cent of the migraine cases I examined. I feel that this sign is so common that if corroborated it will eventually aid physicians in making a diagnosis.

The Horseshoe Symbol

The sign which was found to occur commonly in migraine patients can be described as follows:

A flat space or concave pouch, resembling a horseshoe, is observed between the eyebrows, just above the base of the nose. This area, comparatively free from creases, is slightly wider at the top than at the bottom, thus the horseshoe shape. The tip of the little finger fits into this space in many cases. In others it may be just a flat area.

I have made it a routine to look for this sign in all patients with gastrointestinal complaints in addition to a history of unilateral headaches. They are asked simply to wrinkle their forehead upward. If the history obtained is typical of migraine, and if the patient's headaches can be relieved by Gynergen, D.H.E. 45 (Sandoz), or if the sign is present, a positive diagnosis of migraine is assured in more than 88 per cent of these patients.

It is again emphasized that most of my patients come to me originally with gastrointestinal complaints. Some of these are migraine sufferers while others are not. The use of the diagnostic horseshoe symbol is to simplify the diagnosis of migraine and to help me scan those patients that are probably migraine sufferers.

Table I lists the patients who came to me with gastrointestinal complaints, had the sign and were then proven to be cases of migraine. All of them responded to Gynergen and many were found to be allergic to certain foods. Only 12 per cent did not have the sign.

TABLE I

PRESENCE OF SIGN IN PATIENTS WITH MIGRAINE

Patient	Sex	Age	Proven Case	Response to Gynergen	Migraine Sign
C.R.	F	56	Yes	Yes	Yes
M.B.	F	19	"	"	No
E.T.	F	38	"	"	Yes
H.O.	M	34	"	"	Yes
C.H.	F	37	"	"	Yes
M.P.	M	33	"	"	Yes
F.P.	F	47	"	"	Yes
S.R.	M	32	"	"	Yes
B.M.	F	45	"	"	Yes
N.S.	F	32	"	"	Yes
R.M.	M	42	"	"	Yes
H.M.	F	54	"	"	Yes
A.L.	M	45	"	"	Yes
E.T.	F	41	"	"	No
E.S.	F	27	"	"	Yes
E.C.	M	31	"	"	Yes
C.V.	F	40	"	"	Yes
R.C.	M	33	"	"	Yes
H.G.	F	47	"	"	Yes
M.B.	F	54	"	"	Yes
P.P.	F	53	"	"	No
H.M.	M	53	"	"	Yes
K.J.	F	25	"	"	Yes
M.C.	M	31	"	"	Yes
A.B.	M	61	"	"	Yes

12 per cent of these cases did not have the sign.

Table II lists the patients that came to me with gastrointestinal complaints and who were examined for the sign. They were not migraine sufferers and yet 16 per cent showed the sign with no history of migraine. It is obvious then that the sign can be relied upon in about 84 to 88 per cent of the patients with gastrointestinal complaints and migraine. I again emphasize that all of these cases were taken at

TABLE II

PRESENCE OF SIGN IN PATIENTS WITHOUT HEADACHES

Patient	Sex	Headache	Sign
M.D.	F	No	No
W.G.	M	No	Yes
J.G.	M	No	No
A.T.	M	No	No
W.D.	F	No	No
F.O.	F	No	No
J.H.	F	No	No
T.S.	M	No	Yes
M.D.	F	No	No
V.N.	F	No	No
E.A.	M	No	No
J.K.	M	No	Yes
B.K.	M	No	No
D.D.	F	No	No
F.B.	M	No	No
A.M.	F	No	No
H.D.	M	No	No
R.C.	F	No	Yes
G.B.	M	No	No
M.K.	M	No	No
A.F.	F	No	No
A.L.	M	No	No
W.C.	M	No	No
J.M.	F	No	No
R.H.	F	No	No

16 per cent of these cases had the sign.

random from my practice and that I present these facts as an additional criteria to aid the diagnosis of migraine.

The following case histories are also taken from my files at random with the pictures of the patients.

Case 1:—A.L. This 45-year old male states he has had occasional headaches since adolescence, but during the last five years his headaches have become pro-

Fig. 1

Fig. 2

Fig. 1—Shows the patient without wrinkling the forehead.
Fig. 2—Shows the Migraine Sign after patient has wrinkled his forehead upward.

gressively worse. They are usually unilateral, and occur at least once a week. The headaches extend from the frontal to the occipital region and cause a burning or stabbing pain through the eye. They are accompanied by nausea and vomiting at times, and seem to come on when the patient is constipated. He has taken laxatives and occasional enemas to obtain relief. Certain foods, such as cabbage and sauerkraut, upset him, causing gas and distress. Family history reveals that his mother

Fig. 3—Shows close view of the forehead with the patient wrinkling her forehead upward, revealing the Migraine Sign.

had severe headaches, and that his daughter also suffers from a similar type of headache accompanied by gastrointestinal disturbances. His weight is 150 lbs. and blood pressure is normal. Physical examination was essentially negative, except for the presence of the Migraine Sign. All other tests and examinations were found to be normal.

Case 2:—N.S. This 32-year old female states that she has had unilateral headaches since adolescence. At the age of 14 she had a ruptured appendix with peritonitis, and in 1936 had a sinus operation. In 1937 she had her tonsils and adenoids removed. About 5 years ago she was treated for indigestion which resulted from a diseased gallbladder with stones. A cholestectomy was performed in 1943, and at that time many adhesions were found and separated. Despite this operation, the headaches, nausea and vomiting continued. On physical examination in 1948, the salient signs were—horseshoe sign of migraine on the forehead, slightly coated tongue, scaphoid abdomen with extreme tenderness in the midline just below the umbilicus over a well healed scar from the previous operation. Vaginal examination revealed some retroversion of the uterus, but it was freely movable. Gastric analysis, blood count, sedimentation rate and stool studies were all negative. The patient is a high-strung type of individual, very exacting, a so-called "perfectionist", and of the

Fig. 4—Shows the typical Migraine Sign in patients with headaches due to migraine.

definite psychic pattern so often seen in migraine cases. A second operation for adhesions was performed, but the headaches continued.

Case 3:—R.M. This 48-year old male states that he has had unilateral headaches since adolescence. The headaches usually are accompanied by nausea and vomiting. The patient observed that certain foods bring on these headaches. He has therefore learned to avoid chocolate, creamed and fried foods. He has for many years taken laxatives to relieve constipation since he noticed that the headaches were more severe when he was constipated.

This patient was first seen in 1949, at which time the Migraine Sign was found on physical examination. There also was some tenderness noted in the abdomen to the right of the umbilicus. A rectal fissure was also present. Blood count, sedimentation rate and gastric analysis were all found to be within normal limits. A G.I.

series, performed at Mountainside Hospital revealed the presence of a duodenal ulcer. A gallbladder series and barium enema were both negative. The patient was treated for the duodenal ulcer and has showed improvement. He now occasionally has unilateral headaches and some nausea, but little vomiting.

In recent literature the concurrence of migraine with peptic ulcer, according to Kleckner and Horton[2] occurs in 3.1 per cent of their cases.

Case 4:—This case, whom I will call "Carl", was discovered by me while on a cruise. Carl was a waiter on the boat and while he was waiting on our table I observed the Migraine Sign on his forehead. He confirmed a typical history of migraine.

The use of diagnostic tests greatly facilitates the making of a diagnosis. The diagnosis of migraine has been complicated by the fact that many of the patients

Fig. 5—Shows Migraine Sign.

stress the abdominal complaints rather than the unilateral headache. The identification of the horseshoe symbol in migraine will greatly facilitate the recognizing of this condition.

Summary

1. Any objective evidence of disease simplifies the task of diagnosis.

2. A new sign for the diagnosis of migraine is described. It has been observed in over 88 per cent of my migrainous patients.

3. Four case histories are given in which the "horseshoe" was observed. Illustrations are included.

4. This sign, together with the history, relief of pain with Gynergen, D.H.E. 45 or negative pathological findings, will enable the physician to make a diagnosis of migraine in 88 per cent of these cases.

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DEODORIZATION OF COLOSTOMIES WITH CHLOROPHYLL

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One of the most distressing sequelae of a colostomy, both to the patient himself and to those in proximity to him, is the odor emanating from the colostomy which is so difficult to control. During the period of hospitalization, ward patients with a colostomy are unwelcome neighbors, and in semiprivate rooms it is not unusual for an occupant of an adjoining bed to request a transfer to other accommodations. After discharge from the hospital, a problem of morale often presents itself, the patient hesitating to resume his old way of life with the inevitable close contacts with others. At home, in the office, at social gatherings, he may be self-conscious and apprehensive for fear of "offending". Control of this unhappy situation is an important aspect of the patient's rehabilitation.

In 1947, Bowers[1] reported the effects of water-soluble chlorophyll preparations in wound healing. Throughout his paper reference is made to the deodorizing action of chlorophyll, particularly in connection with cases of osteomyelitis with wide-open malodorous wounds. Bowers states, "Our first observation on beginning use of chlorophyll was that this odor immediately disappeared. Soon, other patients in the neighboring beds began to request treatment with the 'green medicine' because they, too, observed the rapid progress after months of drainage and odor." Subsequently other reports[2,3,4] suggested that certain chlorophyll preparations taken internally were effective in controlling odors of systemic origin. Rapp[5] using water-soluble chlorophyll derivatives taken orally in tablet form, obtained effective deodorization of breath, body, and urine odors. No untoward effects were noted in connection with the use of any of these preparations.

In view of these observations, it seemed possible that chlorophyll taken orally and in sufficient quantity might prove helpful in the control of colostomy odors, and an investigation of this possibility was undertaken. In the belief that the type of chlorophyll used might have an important bearing on the degree of success attained, we chose what appeared to be chlorophyll in its most readily utilized form: a highly concentrated, water-soluble chlorophyll derivative in tablet form, palatable and readily soluble in the saliva medium†.

These tablets were administered to eight ward and semiprivate patients with colostomies, in a dosage of from four to eight tablets daily. Within forty-eight hours there was a striking reduction in objectionable odor, to the gratification of

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†The tablets were supplied by the Rystan Company, Inc. of Mt. Vernon, New York, and are marketed under the trade name of Chloresium Tablets.

not only the patients themselves but also of staff members and other patients in the ward and adjoining beds.

Case Reports

It seems unnecessary to present the details of all patients since the results were uniform. The following cases are representative:

Case 1:—A. A., a 32-year old housewife, was admitted to the ward with a history of rectal bleeding for two weeks. Examination revealed a large polypoid mass in the rectum, three inches above the anus. Biopsy showed adenocarcinoma, and an abdominoperineal resection was performed. On the fourth postoperative day, the patient commenced to have fecal discharges via the colostomy. On the seventh postoperative day, chloresium was administered, one tablet four times daily. Within 48 hours there was a noticeable decrease in the odor of the stools. The dose was increased to two tablets four times daily and 24 hours later there was no fecal odor whatsoever. The color of the stools was dark green and the consistency was normal.

Case 2:—M. E., a 57-year old female, was admitted to a semiprivate room with a two-months' history of increasing constipation and abdominal pain. A palpable mass was felt in the left lower quadrant. Barium enema revealed a lesion of the proximal sigmoid. An obstructive resection was done because of the marked discrepancy in lumen of the proximal and distal segments of the colon. The proximal clamp was removed 48 hours postoperatively and on the fifth postoperative day, a large, foul-smelling, brown stool was passed. The patient complained bitterly of the persistent fecal odor about her and was especially distressed when she overheard the patient in the next bed remark about the odor. Two tablets of chloresium were given four times daily. Within 24 hours her stools turned green and completely lost their fecal odor. There was a noticeable improvement in the patient's attitude and morale. Although she was aware that her colostomy was to be a temporary one, the deodorization of the stool rendered the period during which her colostomy was open much less disagreeable.

Case 3:—M. Z., a 27-year old male, was admitted to the ward with a palpable rectal carcinoma in addition to congenital multiple polyposis of the colon. As a first stage procedure, an abdominoperineal resection was performed. On the sixth postoperative day, the colostomy began to function. For three days he passed a large amount of gas and feces. His neighbors were cognizant that a "colostomy case" was in their cubicle. The patient was given two chloresium tablets four times daily. The decrease in the fecal odor was gradual. However, in two days the odor completely disappeared and on discharge from the hospital he requested a continuation of the medication.

Similar results were obtained in all other patients. It was found that while one tablet of chloresium four times daily would gradually reduce and eliminate the odor of the colostomy discharge, eight tablets daily produced the most rapid and complete effect.

A logical extension of these observations is that the use of chloresium tablets could effectively eliminate bed pan odors in nonsurgical patients who are in close

proximity, and serve to make their hospitalization a more pleasant experience both for them and the hospital attendants.

Summary

1. In an attempt to eliminate the unpleasant odor emanating from colostomy discharges, a water-soluble chlorophyll preparation was administered orally in a dose of four to eight tablets daily.

2. The results were uniformly good to the gratification of the patient, his neighbors and the hospital staff.

3. It is suggested that this medication may be employed to eliminate bed pan odors in nonsurgical patients.

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NONSPECIFIC REGIONAL JEJUNITIS

Case Report

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"Regional ileitis" was first described as a clinical entity in 1932 by Crohn, Ginzburg and Oppenheimer[1]. In 1941 Crohn and Yunich[2] reporting on 200 cases described involvement of the upper ileum or jejunum, as well as the lower segments of the bowel, in 17 of these cases; the disease was limited to the upper ileum and jejunum in 5 of the 17 cases; but in no instance was the disease entirely confined to the jejunum! In 1933, Harris, Bell and Brunn[3] described the first case in which the jejunum was the sole site of involvement. Several cases[4-9] have been reported since that time but in a number so small as to make this entity of "nonspecific regional jejunitis" a clinical rarity.

Browne and McHardy[10] found no instance of the disease in more than a million hospital admissions including 8,000 autopsies. Brown and Donald[11] reviewed 178 cases of regional ileitis at the Mayo Clinic between 1922 and 1940 and found only 5 cases of disease confined to the jejunum. In a recent report on "cicatrizing enteritis" by Nickel[8] one instance was described in 51 cases admitted to the New York Hospital between 1937 and 1949.

We are presenting a case from our surgical practice as an additional contribution to the meager literature on this interesting clinical entity.

A white female, a registered nurse, aged 21, was admitted to Monmouth Memorial Hospital, Long Branch, N. J., on May 30, 1949, with abdominal cramps and distention, and watery bowel movements of one week's duration, and vomiting of two days' duration. The patient had suffered from constipation prior to the onset of the admitting symptoms. The past history disclosed tonsillectomy and adenoidectomy as a child, appendectomy and excision of a cyst from the right ovary in December, 1946, and lysis of postoperative adhesions for relief of a partial intestinal obstruction in October, 1947. The menstrual cycle had been irregular since the ovarian surgery and, following a miscarriage at eight weeks in October, 1948, she menstruated in January, 1949, for the last time prior to admission. Physical examination revealed a temperature of 98.6°F. (oral), pulse rate of 96, respiratory rate of 22, and a blood pressure of 118 systolic and 68 diastolic. The abdomen was moderately distended and tympanitic, tender in the right lower quadrant with absent rebound phenomenon, and presented no masses or enlarged organs. Peristalsis was auscultable. Rectal examination was negative and bimanual pelvic examination disclosed a soft, symmetrically enlarged uterus the size of a four-month pregnancy. A moderate nonpitting edema of the ankles was observed. Urinalysis was negative. The blood showed 12.5 grams of hemoglobin and 7,600 leucocytes with 68 per cent polymorphonuclear and 32 per cent lymphocytes. A scout film of

the abdomen revealed large and small intestinal obstruction with one loop of small intestine in the left mid-abdomen showing no mucosal pattern (gangrenous?).

With a preoperative diagnosis of "partial intestinal obstruction due to postoperative adhesions", operation was performed on the day of admission, with the patient under spinal anesthesia. A left lower paramedian incision was extended upward to disclose the pathology found. Approximately 60 centimeters of jejunum distal to the ligament of Treitz was thick, edematous and slightly discolored with a dark and congested mesentery. A large number of enlarged mesenteric glands were present. The peritoneal cavity contained 200 c.c. of pink-colored, turbid fluid. The uterus resembled a four-month pregnancy.

Postoperative recovery was rapid and uneventful. The temperature did not rise above normal. The patient was ambulatory in 24 hours. Her bowels moved spontaneously on the fourth day and a regular diet was easily taken by that time. She received multiple vitamin therapy, 300,000 units of procaine penicillin G in aqueous solution twice daily until the tenth day, and 0.5 grams of dihydrostreptomycin every six hours until the sixth day. The skin clips were removed on the sixth day and healing occurred per primam. A pregnancy test was positive on the seventh postoperative day and a gastrointestinal roentgenogram on the eleventh day was completely negative; a breech fetus of five-months gestation was visible.

The patient subsequently delivered a normal full-term infant after an uneventful pregnancy and has been asymptomatic to this date, two years postoperative.

Comment

This case well illustrates the clinical findings observed in most of the cases previously reported. The operative findings were those of nonspecific regional jejunitis in a 60 cm. segment of proximal jejunum. The absence of roentgenographic evidence postoperatively after typical preoperative findings is also in keeping with other cases x-rayed before and after surgery. However, unlike those cases reviewed, neither resection of the involved segment of jejunum nor a short-circuiting type of operation was performed; exploration and identification of the pathological process without further surgery resulted in rapid and complete relief from symptoms. This may represent an acute or subacute process rather than the chronic type of "regional enteritis" or "cicatrizing enteritis" usually described. Although this entity has probably been described in the female, in those cases reviewed no instance in the female was reported so that the incidence is certainly uncommon.

Summary and Conclusions

An additional case of nonspecific regional jejunitis is reported. Unusual features are the occurrence in a female, its lack of chronicity, and the treatment without surgically altering the gastrointestinal continuity.

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A HIGHLY POTENT

LIPOTROPIC COMBINATION

Solution

SIRNOSITOL

CHOLINE AND INOSITOL

With Solution Sirnositol, lipotropic therapy can be put on a sound basis. This new lipotropic combination permits adequate dosage to be administered, enhancing the efficacy of therapy.

✓ ***CONCENTRATED.*** Each tablespoonful (15 cc.) of Sirnositol contains 7.41 Gm. of choline gluconate (equivalent to 3.0 Gm. of choline base) and 0.75 Gm. of inositol. This quantity given three times daily provides a good dosage of each active ingredient.

✓ ***PALATABLE.*** The choline gluconate and inositol have been dissolved in a pleasantly flavored, sugar-free, aqueous vehicle.

AVAILABILITY

Solution Sirnositol is supplied in 1 pint bottles and is available on prescription through all pharmacies.

✓ ***WIDELY USEFUL.*** Solution Sirnositol is indicated whenever lipotropic therapy is required—in many hepatic derangements, atherosclerosis, and prophylactically in coronary sclerosis.

C.S.C. Pharmaceuticals **A DIVISION OF**

COMMERCIAL SOLVENTS CORP., 17 E. 42nd ST., NEW YORK 17, N.Y.

No belladonna backfire...

when you relieve nervous indigestion with.....

[redacted]

Clinical [1,2,3] and pharmacological results show that the dual action of BENTYL (musculotropic, neurotropic) provides complete and more comfortable relief than that of all other antispasmodics tested.

DOSAGE: Two capsules three times daily, before or after meals. If necessary, repeat dose at bedtime.

BENTYL .....10 mg.
for comfortable relief of nervous indigestion

BENTYL .....10 mg.
with **PHENOBARBITAL**.....15 mg.
when synergistic sedation is desired

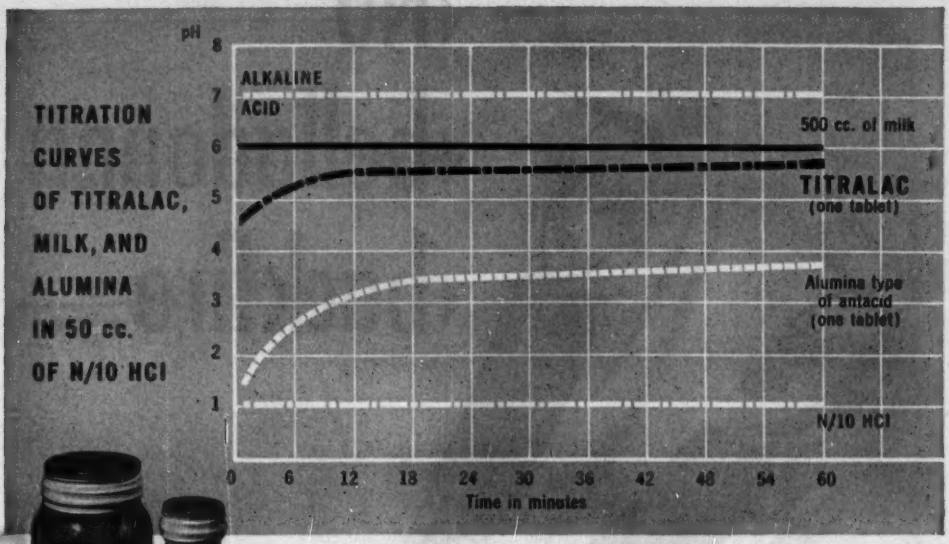
1. Hock, C.W.: J. Med. Assn. Ga. 40: Jan., 1951
2. Hufford, A.R.: J. Mich. St. Med. Soc. 49:1308, 1950
3. Chamberlin, D.T.: Gastroenterology 17: Feb., 1951

Merrell 1828

Trade-mark "Bentyl" Hydrochloride

New York — CINCINNATI — Toronto

NON-SURGICAL TREATMENT



OF PEPTIC ULCER

Gastroenterologists have long endorsed the use of milk, when practicable, for its ideal acid-converting power and buffering capacity.[1, 2] In a recent comprehensive paper, Aaron[3] and others[4, 5, 6] express a preference for calcium carbonate as the antacid to be employed.

TITRALAC, by combining proper proportions of purified calcium carbonate and the amino acid glycine, *provides an acid-converting and buffering effect practically equivalent to that of fresh milk*, as shown in the above chart.* Just 1 TITRALAC tablet is equivalent to an 8-ounce glass of milk in antacid effect and provides quick and long-lasting relief from the distressing symptoms of hyperacidity.

The very agreeable taste of soft-massed TITRALAC tablets, which is achieved without employing taste-disguising, acid-generating sugars in the formula, makes them as acceptable to patients as a mint after dinner. Prescribing TITRALAC eliminates the probability of unfavorable reactions often associated with the taking of metallic-tasting, astringent tablets or liquids, and ensures adherence to the prescribed dosage.

TITRALAC tablets are supplied in bottles of 100 and convenient-to-carry packages of 40. TITRALAC powder is also available, in 4-oz. jars.

REFERENCES

1. Rossett, N. E., and Flexner, J.: Ann. Int. Med. 18: 193 (1944). 2. Freezer, C. R. E.; Gibson, C. S., and Matthews, E.: Guy's Hosp. Reports 78: 191 (1928). 3. Aaron, A. H.; Lipp, W. F., and Milch, E.: J. A. M. A. 139: 514 (Feb. 19) 1949. 4. Kirsner, J. B., and Palmer, W. L.: Illinois M. J. 94: 357 (Dec.) 1948. 5. Kimball, S.: in Practice of Medicine (Tice). Hagerstown, Md., W. F. Prior Company, Inc., 1948; p. 210. 6. Special Article: M. Times 76: 10 (Jan.) 1948.

*The formula of TITRALAC is one whose composition and mode of action are recognized by U.S. Patent No. 2,429,396.

Samples and literature to physicians upon request.

SCHENLEY LABORATORIES, INC., 350 FIFTH AVENUE, NEW YORK 1, N. Y.

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Administration of Cremothalidine to provide bacteriostatic effect after intra-abdominal surgery.

PHYSICIAN, PATIENT PREFER THIS "SULFA" SUSPENSION

Many physicians prefer CREMOTHALIDINE® for providing bacteriostatic effect in *intestinal* disorders because it contains Sulfathalidine® *phthalyl*sulfathiazole in a fine state of subdivision maintained by fluid dispersion. Sulfathalidine acts largely *within the intestine* because it is absorbed to the extent of only about five per cent. This "localized" action makes it possible to maintain high bacteriostatic concentration in bowel contents—and to avoid building up needlessly high systemic levels of the drug.

Many patients prefer CREMOTHALIDINE because it is so pleasant to take, and so easy to swallow. Its smoothness and its distinctive flavor make it attractive to patients of all ages. Because of its *fluid form* and its *pleasing taste* it is well suited for administration to children—and to adults with gastrointestinal "upsets."

Indications CREMOTHALIDINE is indicated in inflammatory conditions of the colon; as an adjunct in the management of ulcerative colitis; for use before and after colon surgery, to reduce risk of peritonitis.

Average Dose for adults: 1 to 2 teaspoonfuls four times daily. For children: ½ to 1 teaspoonful four times daily. For infants: ½ to 1 teaspoonful three times daily.

Packaging CREMOTHALIDINE is supplied in Spasaver® bottles of 8 fluidounces. Sharp & Dohme, Philadelphia 1, Pa.

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Sulfathalidine® Suspension

New Form of Levo-Alkaloids of Belladonna For Selective Spasmolytic Action

The practical value of an antispasmodic depends upon the degree of a desirable spasmolytic effect, convenience of administration and patient acceptability.

Degree of spasmolytic effect of belladonna alkaloids rests upon the intensity of parasympathetic inhibition. Pure levorotatory belladonna alkaloids (Bellafoline) are more potent and selective than belladonna alkaloid mixtures in producing this spasmolytic effect, at the same time minimizing the undesirable cerebrospinal effects.

Studies by *Kramer and Ingelfinger*, (M. Clin. North Amer., Boston No.: 1227, (1948) demonstrate the highly efficient action of Bellafoline. By balloon-kymograph studies on the human intestine they found that most commonly used antispasmodics are less effective than atropine (standard dose: 1/100 gr.). Bellafoline was the outstanding exception. It surpassed atropine in both degree and duration of action.

The antispasmodic effect of Bellafoline is augmented by a small dose of phenobarbital thereby reducing underlying excitability and tension.

Such an association of Bellafoline and phenobarbital is *now available in the form of Elixir Belladenal.*

Thus Elixir Belladenal fulfills the requirements for practicality by reason of: high efficacy, patient acceptance, convenience of dosage regulation. It is especially serviceable in pediatrics and in those adults where the use of tablets is impractical. The teaspoonful dose contains Bellafoline (levorotatory alkaloids of belladonna leaf) 0.0625 mg. and Phenobarbital 12.5 mg. The indications are those of Belladenal Tablets, e.g. Peptic ulcer, Pseudo-ulcer, Spastic colon, other hypermotility-hypersecretion states of the gastrointestinal-biliary tracts and genito-urinary spasm. Professional Samples and Literature available upon request.

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In diarrheas, Kaopectate* acts as a "liquid magnet", adsorbing and removing bacteria and toxins. At the same time it coats and protects irritated intestinal mucosa, and it consolidates watery stools. For the common diarrheas (e.g. those associated with dietary indiscretions and food spoilage).

℞ ***Kaopectate****

Each fluidounce contains:

Kaolin ... 30 grs.

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Available in 10 fluidounce ...

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Phospho-Soda (Fleet) has long been authoritatively recognized for its dependable efficacy and desirable qualities in the treatment of intestinal stasis. In average doses, it produces a soft and formed, rather than a watery, evacuation; and its gentle action is quite free from irritation, griping, early tendency toward habituation, or other adverse reactions. Samples on request.

Phospho-Soda (Fleet) is a solution containing in each 100 cc sodium biphosphate 48 Gm. and sodium phosphate 18 Gm. Both Phospho-Soda and Fleet are registered trademarks of C. B. Fleet Co., Inc.

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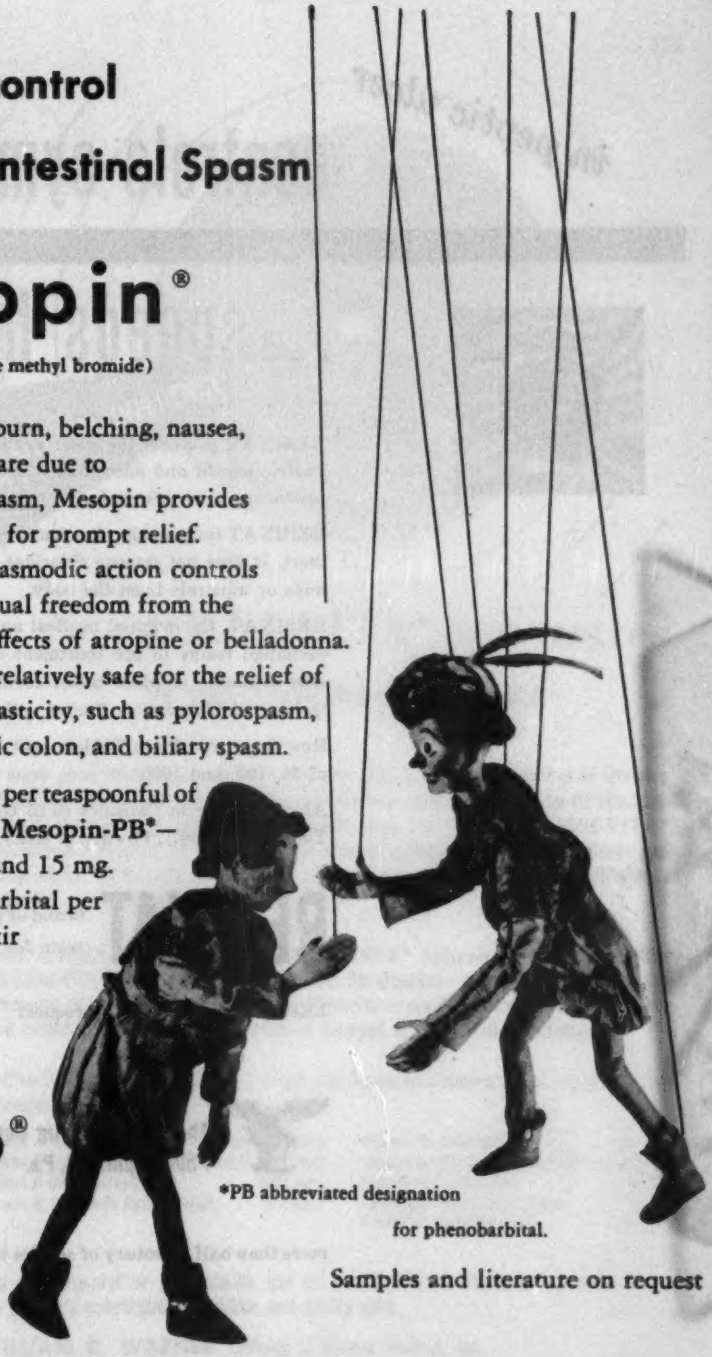
selective control of Gastrointestinal Spasm

Mesopin®

(brand of homatropine methyl bromide)

When pain, heartburn, belching, nausea, or unstable colon are due to gastrointestinal spasm, Mesopin provides an effective means for prompt relief. Its selective antispasmodic action controls spasticity with virtual freedom from the undesirable side effects of atropine or belladonna. Thus, Mesopin is relatively safe for the relief of gastrointestinal spasticity, such as pylorospasm, cardiospasm, spastic colon, and biliary spasm.

Mesopin—2.5 mg. per teaspoonful of elixir or per tablet. **Mesopin-PB***—2.5 mg. Mesopin and 15 mg. (1/4 gr.) phenobarbital per teaspoonful of elixir or per tablet.



Endo®

*PB abbreviated designation for phenobarbital.

Samples and literature on request

Endo Products, Inc., Richmond Hill 18, N. Y.

in peptic ulcer

controls symptoms

...speeds healing

RESINAT protects the ulcer crater by inactivating gastric pepsin and adsorbing excess acidity, without producing acid rebound or systemic alkalinization.

RESINAT is insoluble, chemically and physiologically inert. It does not remove chlorides, phosphates, vitamins or minerals from the body.

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For many years, much time and effort has been given to the development of an effective multivitamin preparation which would not frighten or repel the patient by its size, disagreeable taste or odor, and unpleasant appearance. The stability of OMNI-VITA* Spherettes is assured by layering of the vitamin components. Younger patients and finicky adults, particularly, were likely to object strenuously to the average multivitamin preparation—oils, liquids, tablets, or capsules.

Warner is proud, therefore, to present OMNI-VITA* Spherettes. A delicious, chewable Spherette containing generous amounts of the vitamins—an excellent and extremely convenient means for supplying either supplemental or prophylactic doses of the vitamins most frequently low in the modern diet or involved in subclinical deficiencies.

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Vitamin A, Synthetic	5,000 U.S.P. Units	Vitamin B_2 (Riboflavin)	2.0 mgs.
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Vitamin C (Ascorbic Acid)	50.0 mgs.	Vitamin B_{12}, Crystalline	1.0 mcg.
Vitamin B_1 (Thiamine Hydrochloride)	1.0 mg.	Panthenol (equiv. to 1.15 mgs. d-Calcium Pantothenate)	1.0 mg.

The supplemental or prophylactic use of OMNI-VITA* Spherettes ensures the the patient's cooperation—children and adults alike.

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For Uncomplicated Ulcer AMPHOJEL provides "double gel" action: the quickly reacting antacid gel, and the prolonged local protection of the demulcent gel.

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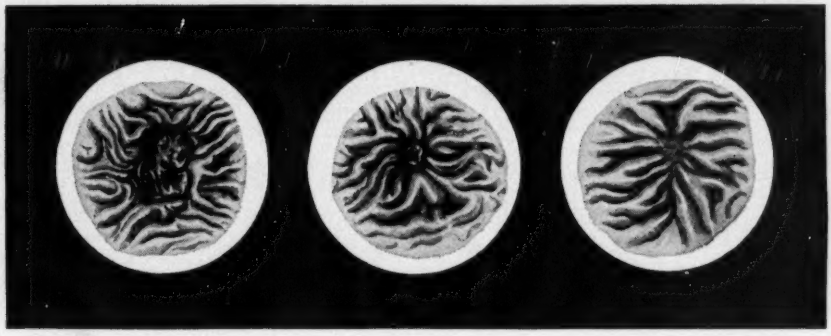

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